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ORIGINAL ARTICLE

A triple-blind, randomized controlled trial on the efficacy and safety of 1.5% *Carica papaya* latex cream vs. 2% ketoconazole cream in the treatment of pityriasis versicolor among Filipinos

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ABSTRACT

BACKGROUND *Carica papaya* latex has been found to have antifungal properties rendering an alternative treatment for fungal infections, i.e. pityriasis versicolor. It has remarkable mycelial inhibition, and static effect on fungal growth in cultures. Its keratolytic effect can remove diseased skin cells, and enhance drug penetration. Moreover, it is organic, locally available, and relatively inexpensive.

OBJECTIVE To compare the efficacy and safety of 1.5% *Carica papaya* latex cream vs. 2% ketoconazole cream in the treatment of pityriasis versicolor among Filipinos.

METHODS A single-center, parallel group, triple-blind, randomized controlled trial in the Dermatology out-patient clinic of Makati Medical Center was conducted. Sixty-four patients with pityriasis versicolor were randomly allocated to the two treatment groups, and received either 1.5% *Carica papaya* latex cream or 2% ketoconazole cream that they used twice daily for four weeks or until cured. The participants, researcher, and assessor were blinded to the treatment assignments. Therapeutic response was assessed at weeks 1, 2, 3 and 4 based on clinical and mycologic cure. Adverse events were identified. Patients' assessment of their improvement was done at the end of the treatment.

RESULTS All 64 subjects in both treatment groups (100% in the *Carica papaya* and 100% in the ketoconazole group) achieved clinical and mycologic cure within the four-week study period. The adverse reactions noted (pruritus and erythema for *Carica papaya* latex cream, and pruritus for ketoconazole cream) were mild, did not cause disruption of daily activities, and spontaneously resolved.

CONCLUSION 1.5% *Carica papaya* latex cream is an effective and safe alternative treatment to the first line therapy, ketoconazole cream, for pityriasis versicolor.

KEYWORDS Carica papaya, pityriasis/tinea versicolor

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INTRODUCTION

Superficial fungal infections are among the most common infections in the world with incidence rates increasing significantly over the last 15 to 20 years. This infection, known as tinea, has many types, one being tinea versicolor or pityriasis versicolor. Pityriasis versicolor is a common dermatosis in tropical regions like the Philippines, where high humidity and temperature increase its prevalence.[1] A study done by Handog, et al in 2005 showed that fungal infections has a prevalence of 12.98%, and is the second leading cause of consultation in dermatology training institutions in the Philippines, with pityriasis versicolor as the leading diagnosis (25.34%), followed by tinea corporis (22.63%), and tinea cruris (16.7%).[2]

Pityriasis versicolor is a chronic, superficial fungal infection, characterized by changes in skin pigmentation due to the colonization of the stratum corneum by Malassezia furfur, a dimorphic lipophilic fungus. The azelaic acid produced by the organism inhibits pigment transfer to keratinocytes, making infected skin more demarcated from the uninfected, more heavily pigmented skin.[3] Patients present with multiple oval to round patches with mild, fine, scaly lesions that are often confluent centrally. Seborrheic regions are the favored sites of this organism.[4] Versicolor refers to the variety in changing shades of colors present in this disease.

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Pityriasis versicolor occurs most commonly in adolescents and young adults.[3] This may be because adolescents have increased sebum production, leading to easier growth by the lipophilic fungi.[1] It is usually asymptomatic but the appearance may lead to significant emotional distress, particularly in adolescents, and thus needs to be addressed.[5]

Patients with pityriasis versicolor are usually treated with topical antimycotics like ketoconazole (1% or 2%), or 2.5% selenium sulfide shampoo. In the study done by Muzaffar, et al (2008), they identified topical antifungals as the established first line of therapy.[6] Other treatment options include: azole/allylamine creams and lotions, nystatin, salicylic acid, and dandruff shampoos. Systemic therapy with ketoconazole, fluconazole or itraconazole can also be used.[4]

Despite treatment, the rate of recurrence of pityriasis versicolor is very high, especially in hot humid climates, like the Philippines.[4] It is a relapsing disease that tends to recur in about 60% within one year after treatment and in 80% after two years.[1] This is addressed by giving ketoconazole shampoo once weekly as a body cleanser, or once-monthly dosing of oral ketoconazole (400 mg), fluconazole (300 mg), or itraconazole (400 mg).[4] However, these medications can have serious side effects,i.e. hepatotoxicity, and ventricular dysrhythmias.[5] Thus, the use of herbal remedies has become popular since they are generally economical, natural, and safe antifungal remedies without known side effects.[3]

An herbal remedy of growing interest is *Carica papaya*. It is a plant that grows in all tropical and many sub-tropical regions of the world.[7] *Carica papaya* is mainly grown (>90%) and consumed in developing countries, like the Philippines.[7]

Papain is an endolytic plant cysteine protease enzyme isolated from *Carica papaya* latex by cutting the skin of the unripe papaya and then collecting and drying the latex that flows from the cut. The protein ferment papain is the milky substance from the leaves and unripe fruit of papaya.[8] Papain has proven to have many medicinal uses. It has been used as a debris-removing agent, with no harmful effect on sound tissues. It has analgesic, antibacterial, and anti-inflammatory activity. Moreover, papain has been studied for its antifungal properties,[7] thereby rendering a promising alternative treatment for fungal infections such as pityriasis versicolor. In a study by Chukwuemeka & Anthonia in 2012, it has been shown to have remarkable mycelial inhibition with mean zones of inhibitions between 0.23 - 1.73 mm in different fungal isolates like Rhizopus spp., Aspergillus spp., and Mucor spp., supporting its antifungal properties.[9] The review paper by Krishna et al, states that latex has a static effect on fungal growth in cultures. The lytic enzymes on the extracts target the sugar residue on the cell wall of the fungi resulting in cell wall degradation.[8]

In the study done by Buensalido, *Carica papaya* latex extract was found to be superior to ketoconazole and placebo in the treatment of tinea corporis. It was also found to work faster in the clinical resolution of scaling and erythema. Resolution was achieved in 14 days compared to 21 and 28 days in ketoconazole and placebo, respectively.[10]

Another property of papaya that may provide cure for pityriasis versicolor is its keratolytic effect. Some of the established treatments for pityriasis versicolor include keratolytic agents such as selenium sulfide, and salicylic acid. It removes diseased skin cells and replaces them with healthy new cells. Its keratolytic property also tends to improve the delivery of antimycotic drugs through the skin.[1] Thus, it can both give treatment, and enhance its delivery to the affected areas.

With regards to safety, topical papaya fruit has been used as a major component of burn dressings in the Royal Victoria Hospital Pediatric Unit in Quebec, Canada and was found to be safe for use in children.[8] However, it can induce hypersensitivity reaction in individuals with allergy to papaya. It can be an irritant, and a vesicant at certain concentrations. The safe concentration of papain extract that does not produce adverse reactions as determined through patch test was found to be at 1.5%.[10]

With its antifungal, keratolytic, and drug delivery enhancement properties, papain latex extract shows potential in the effective and safe treatment of pityriasis versicolor. This study aims to compare the efficacy and safety of 1.5% *Carica papaya* latex cream vs. 2% ketoconazole cream in the treatment of Filipino patients with pityriasis versicolor. Specifically, this study aims to:

1. To determine and compare the overall clinical cure rate (measured by Grading of Scaling and Pruritus Rating Scale) and mycologic cure rate (through Potassium Hydroxide Smear Mycologic Examination) of pityriasis versicolor patients treated with 1.5% *Carica papaya* latex cream vs. 2% ketoconazole cream, taken weekly for four consecutive weeks
2. To compare the Patient's Assessment of Improvement from Baseline Scale score, taken at the end of the treatment, of those treated with 1.5% *Carica papaya* latex cream vs. those treated with 2% ketoconazole cream
3. To identify any adverse reactions which may occur with the use of 1.5% *Carica papaya* latex cream compared with 2% ketoconazole cream in the course of treatment of pityriasis versicolor, taken weekly for four consecutive weeks, and to compare the Adverse Event Grading Scale of the two treatment groups at the end of the treatment period.

METHODS

STUDY DESIGN

This study assessed the efficacy and safety of 1.5% *Carica papaya* latex cream vs. 2% ketoconazole cream in the treatment of pityriasis versicolor among Filipinos in a randomized, tri-

ple-blind controlled trial. The study was based in the Dermatology Out-Patient Department of Makati Medical Center. The research protocol was approved by the Makati Medical Center Institutional Board Review (MMCIRB 2014-074).

PARTICIPANTS

Participants for this study were Filipino patients of either sex, clinically diagnosed with pityriasis versicolor and confirmed by positive mycologic examination (KOH). Clinical diagnosis was made based on the appearance of hyperpigmented or hypopigmented patches with mild, fine scales.

Subjects under the age of 18 were accompanied by a guardian who read and signed the assent forms. Excluded from this study were patients with extensive involvement (>4 sites; defined as: face, neck, anterior trunk, posterior trunk, upper extremity, lower extremity); size of >3% estimated body surface (size of the face); with concomitant active, localized, or systemic infection; in immunocompromised state; with known or suspected hypersensitivity to any constituent of the medications; pregnant or breastfeeding women. Patients who have used topical and systemic steroids or immunomodulating drugs, keratolytic agents, or topical and systemic antifungals within the last 30 days were likewise excluded.

INTERVENTIONS

The *Carica papaya* latex cream used for this study was patterned after the study made by Buensalido in 2009 but this study used aquaphor and water as vehicle instead of Cetaphil cream. Like in the study of Buensalido, the *Carica papaya* latex cream used in this study was also compounded by the Industrial Technology Development Institute of the Department of Science and Technology (ITDI-DOST), Bicutan, Taguig City.

The study medication was formulated as follows: latex was collected through 1-2mm deep vertical incisions on the skin of the unripe fruit early in the morning as the latex flow is low during the day. The latex is dried at room temperature until crumbly and non-sticky. The dried latex was triturated using a mortar and pestle and sieved through a mesh size 170. The concentration of the papain extract used was 1.5%. The collected latex was stored at 4-8°C until incorporated with the vehicle.[10]

The ketoconazole cream served as the control in this study since it has been proven in literature[11] and in research studies to be an effective treatment for pityriasis versicolor. A clinical study by Bakr et al, in 2020 showed significant improvement in patients with pityriasis versicolor after four weeks of treatment with 2% ketoconazole cream.[12] Like the study medication, the 2% ketoconazole cream from the Pharmaceutical Section of the Chemicals and Energy Division of IDTI-DOST was also mixed with aquaphor and water as vehicle.

Treatment compounds were placed in a container and pre-coded. The pre-coded treatment compounds (labelled with A or B on the container cover) have no significant difference in the consistency, appearance, and smell and were stored in identical 15-gram containers.

OUTCOMES

The primary outcome measure is the therapeutic response, measured by clinical cure rate and mycologic cure rate. Clinical cure rate was assessed using the Grading of Scaling and Pruritus Rating Scale. Mycologic cure rate was assessed using the Potassium Hydroxide Smear Microscopic Examination. Interpretation was based on the amount of hyphae present in the examination.[13]

The secondary outcome measures were the patients' subjective assessment of improvement and the severity of adverse effects measured by the Patients' Assessment of Improvement from Baseline Scale and Adverse Event Grading Scale, respectively.

Therapeutic response was considered a treatment success if all the following conditions were satisfied within the treatment period of four weeks: negative mycologic examination result and absence of pruritus and scaling, defined as score of 0 in the Grading of Scaling, Pruritus Rating Scale, and Potassium Hydroxide Smear Microscopic Examination. In case of treatment failure, the investigator will give immediate and free medical treatment with a standard topical antifungal treatment and will be monitored until resolution of lesions. But in this study, no treatment failure was encountered.

SAMPLE SIZE

Using G Power 3.1.3 for the minimum sample size computation, 40 subjects in each arm were included based on 90% power, 5% level of significance and 0.75 effect size with 20% possible attrition rate.

RANDOMIZATION

The participants, the investigator, and the analyst were not aware of the sequence of group allocations done by the Department of Science and Technology personnel who prepared, pre-coded, and labelled each medication as either A or B. Fishbowl method was done to assign the coded cream to each participant of the study to ensure randomization.

Baseline demographic data were collected and clinical examination of the patient was done by the primary investigator. The clinical presentation of the patient was documented using the Grading of Scaling and Pruritus Rating Scale of the hyperpigmented or hypopigmented patches. A pre-treatment specimen of the lesion was obtained for mycologic examination (KOH smear). Photograph of the skin lesion was taken.

All patients were given instructions on the daily cleansing of the affected area with the standard cleanser provided by the investigator. Patients were instructed to apply the assigned cream (labeled as A or B) over the affected areas two times a day,

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for four weeks using a sterile cotton tip applicator. Patients were instructed to bring the cream container on each follow-up visit to ensure compliance. A set of four 15g cream per container was allotted for each participant throughout the duration of study, but the assigned medication was given one container at a time depending on the amount consumed noted on each follow-up. Patients were asked to do weekly follow-up for four consecutive weeks or until KOH was negative, and pruritus and scaling were absent.

Patients were evaluated at baseline then weeks 1, 2, 3, and 4. On each visit, the investigator evaluated the clinical cure using the Grading of Scaling and Pruritus Rating Scale and the mycologic cure using the Potassium Hydroxide Smear Microscopic Examination. Scales were obtained using the blunt side of a blade from the lesion. Ten percent (10%) potassium hydroxide was used to determine the presence or absence of hyphae. Photograph of the skin lesion was taken at baseline, during each follow-up and at the end of the treatment.

Adverse reactions like irritation, blistering, peeling, urticaria, pruritus, erythema[4] to the site of application were likewise documented at each week of treatment and the Adverse Event Grading Scale of the two groups were compared at the end of the treatment. Patients' subjective assessments were documented using the Assessment of Improvement from Baseline Scale, given at the end of the treatment.

BLINDING

The participants, the investigator, and the analyst were blinded with the treatment assignment. The pre-coded medications were handed by DOST to the investigator and were labelled only with either A or B on the container cover. The treatment compounds have no significant difference in consistency, appearance, and smell and were stored in identical containers.

The investigator recruited the participants, assigned the participants to treatment A or B using fishbowl method, did the weekly assessment, and tabulated the data. The tabulated data were analyzed by an independent statistician. The treatment assignment of the participants were only revealed after data analysis was done.

STATISTICAL ANALYSIS

Intention-to-treat and per protocol analysis were performed. Demographic and clinical data of the two treatment groups were described and compared. Results were presented as distribution

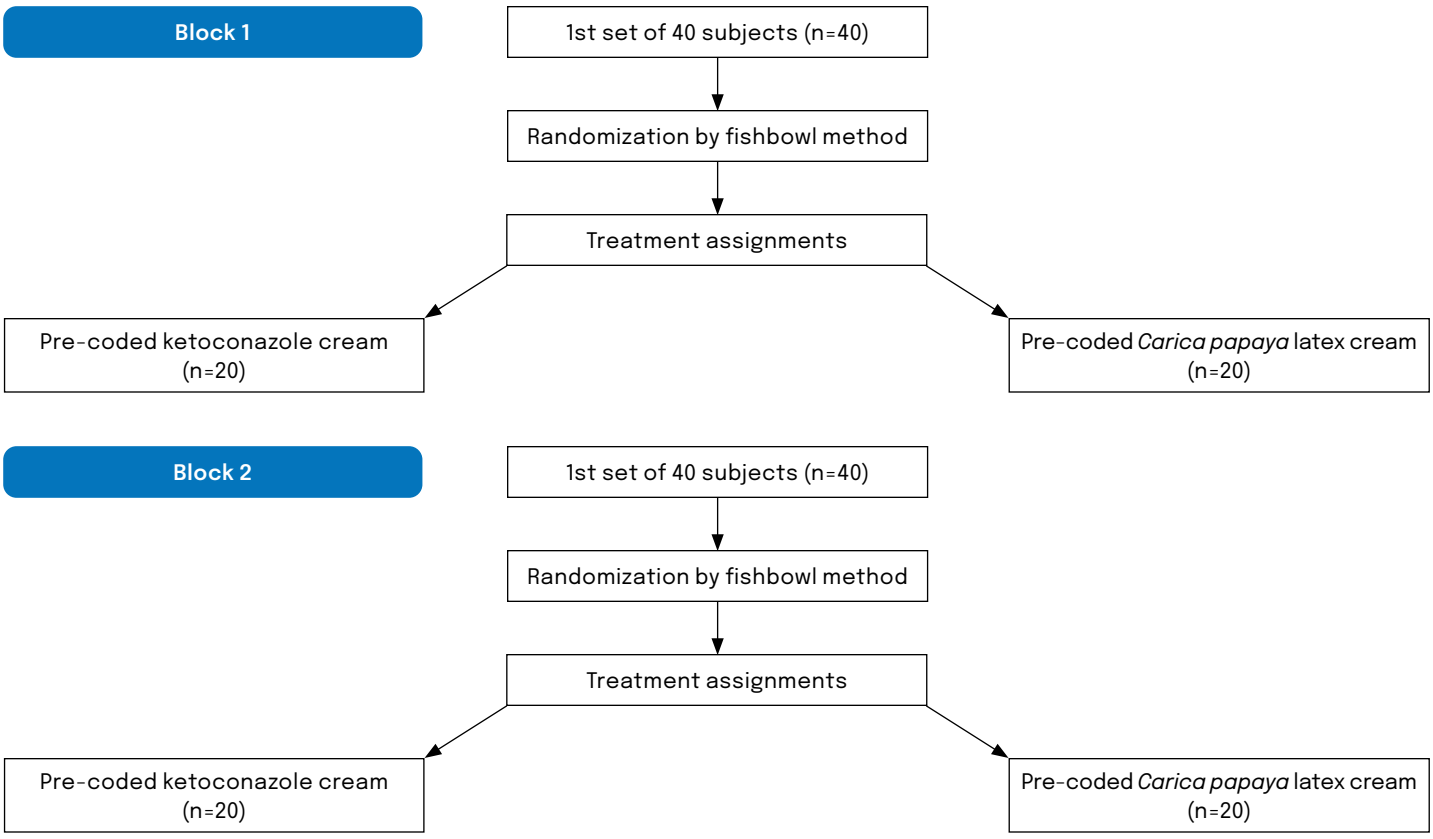

Figure 1. Method of treatment assignment of participants.

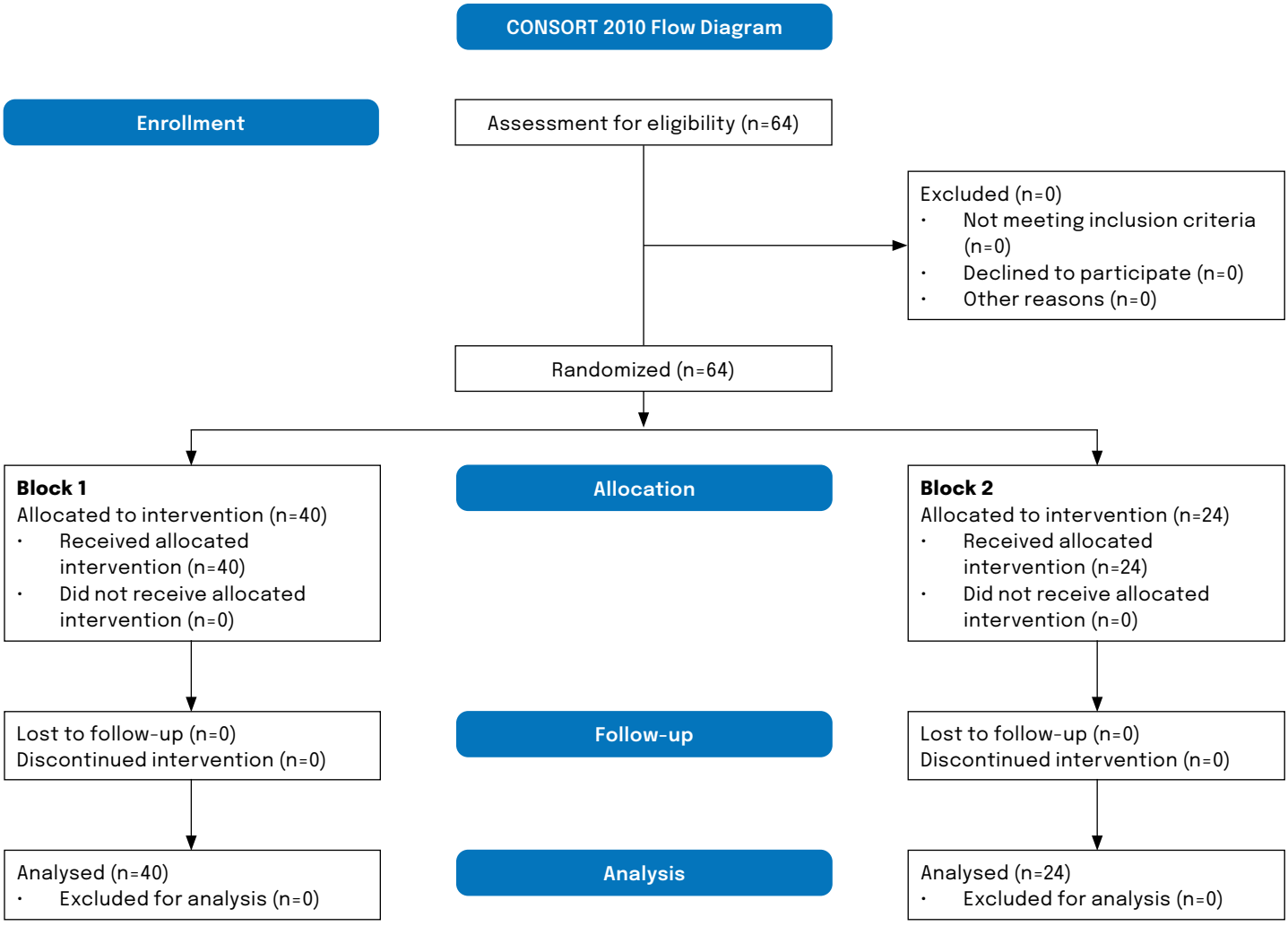

Figure 2. Flow of participants from assessment of eligibility to analysis

frequencies for categorical data and means and standard deviations for continuous data. An independent statistician was hired to conduct the data analysis. Only codes were provided to ensure the blinding of the data analyst.

The comparisons of interest are the efficacy and safety of 1.5% *Carica papaya* latex cream with the standard therapy, 2% ketoconazole cream. Efficacy was analyzed statistically. Comparison on the categorical outcome measures between treatment groups was done by Chi-square.

Adverse events were categorized as a frequency distribution. Counting of adverse events will be based on the number of subjects, not on the number of adverse events. Participants reporting more than one adverse event will be counted only once in the organ system total.

Missing data may be due to drop-outs or withdrawals. Sensitivity analysis using a worst-case scenario was performed to assess the effect of these drop-outs and withdrawals on the conclusion of the study.

RESULTS

A total of 64 patients diagnosed with pityriasis versicolor were included in this study. Sample size of 80 subjects was not met due to lack of eligible patients seen during the recruitment period from May to September 2016.

The demographics of the 64 study patients are shown in Tables 1 and 2. Of the 64 patients, 37 (57%) are male and 27 (43%) are female, with age range of 6-46 years. Majority are students comprising more than half (51%) of the participants. Mean duration of the development of skin lesion is 8.9 weeks, with chest (41.3%) and back (39.1%) as the most affected parts. As stated on the p-value column in Table 2, the 2 groups were not significantly different from each other in terms of the duration

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of their skin lesions. More than a quarter (26.6%) used topical antifungal medication but more than 4 weeks prior to joining the study. None of the participants used any topical or oral corticosteroids, as well as oral antifungal medications.

Primary outcome measure results are shown on Tables 3, 4, and 5. As stated on the p-value column of the tables below, all comparisons made from Week 1 to Week 4 were not significantly different from each other, indicating that there was no significant difference between the two treatments used. The cure rate based on scaling score, pruritus scale, and KOH mycologic examination smear score for both treatments are comparable.

Adverse effects that were reported by the patients participating in the two study groups are tallied and presented in Table 6. In this study, pruritus is the most common adverse event experienced by a patient receiving either treatment A

Table 1. Demographic profile of the patients

Profile	Zinc oxide group (n=15)		Salicylic+Lactic acid group (n=14)		P-value	
	#	%	#	%	#	%
Total	30	46.9	34	53.1	64	100
Age group						
• <11 years old	3	4.7	2	3.1	5	7.8
• 11-20 years old	13	20.3	18	28.1	31	48.4
• 21-30 years old	5	7.8	4	6.3	9	14.1
• 31-40 years old	7	10.9	8	12.5	15	23.4
• >40 years old	2	3.1	2	3.1	4	6.3
Gender						
• Male	19	29.7	18	28.1	37	57
• Female	11	17.2	16	25.0	27	43
Type of Work						
• Student	16	25.0	17	26.6	33	51.6
• Housewife	4	6.3	1	1.6	5	7.8
• Employee (Office work)	3	4.7	6	9.4	9	14.1
• Construction	3	4.7	3	4.7	6	9.4
• Vendor	1	1.6	5	7.8	6	9.4
• Guard	2	3.1	1	1.6	3	4.7
• None	1	1.6	1	1.6	2	3
Affected areas						
• Chest	14	21.9	15	23.4	29	45.3
• Back	13	20.3	12	18.8	25	39.1
• Head	8	12.5	13	20.3	21	32.8
• Upper extremities	9	14.1	7	10.9	16	25.0
• Neck	0	0.0	1	1.6	1	1.6
Use of antifungals						
• Topical	9	14.1	8	12.5	17	26.6
• Oral	0	0.0	0	0	0	0
Use of corticosteroids						
• Topical	0	0.0	0	0.0	0	0.0
• Oral	0	0.0	0	0.0	0	0.0

Table 2. Duration of the lesions.

Treatment	Range	Mean	Standard deviation	P-value
Treatment A (1.5% *Carica papaya* latex cream)	1 - 28 weeks	8.43	7.31	0.425
Treatment B (2% ketoconazole cream)	1 - 20 weeks	9.32	6.48	
Total	1 - 28 weeks	8.91	6.84	

Table 3. Summary of the number of patients per Grading of Scaling Score.

Scaling score	Treatment A (1.5% *Carica papaya* latex cream)			Treatment B (2% ketoconazole cream)			P-value
	0*	1†	2‡	0*	1†	2‡	
Week 0	0	20	10	0	23	11	0.934
Week 1	2	22	6	1	27	6	0.942
Week 2	20	10	0	24	10	0	0.738
Week 3	28	2	0	31	3	0	0.750
Week 4	30	0	0	34	0	0	1.000

*0=no scaling, †1=few scales, ‡2=many scales

Table 4. Summary of the number of patients per Pruritus Scale Score.

Pruritus scale	Treatment A (1.5% *Carica papaya* latex cream)					Treatment B (2% ketoconazole cream)					P-value
	0*	1-3†	4-6‡	7-8§	>9‖	0*	1-3†	4-6‡	7-8§	>9‖	
Week 0	3	15	12	0	0	5	14	15	0	0	0.994
Week 1	7	17	6	0	0	10	20	4	0	0	0.994
Week 2	20	10	0	0	0	22	12	0	0	0	0.873
Week 3	29	1	0	0	0	33	1	0	0	0	0.911
Week 4	30	0	0	0	0	34	0	0	0	0	1.000

*0=no pruritus, †1-3=mild pruritus, ‡4-6=moderate pruritus, §7-8=severe pruritus, ‖>9=very severe pruritus

Table 5. Summary of the number of patients per KOH smear Mycologic Examination score.

KOH Smear Score	Treatment A (1.5% *Carica papaya* latex cream)				Treatment B (2% ketoconazole cream)				P-value
	0*	1†	2‡	3§	0*	1†	2‡	3§	
Week 0	0	9	14	7	0	16	12	6	0.208
Week 1	0	22	8	0	1	24	9	0	0.836
Week 2	9	17	4	0	12	20	2	0	0.444
Week 3	25	5	0	0	29	5	0	0	0.831
Week 4	30	0	0	0	34	0	0	0	1.000

*0= negative (no hyphae), †1= few hyphae (<5 hyphae per high power field), ‡2= moderate hyphae (≥5 but <10 hyphae per high power field), §3= abundant hyphae (≥10 hyphae per high power field)

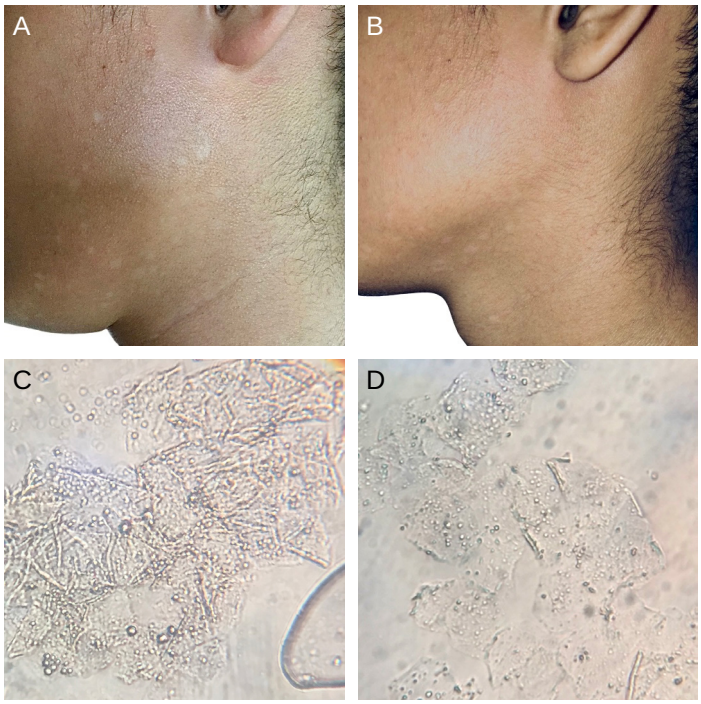

Figure 3. A and C. Representative clinical photo and KOH result of a patient treated with Treatment A (1.5% *Carica papaya* latex cream) at baseline. **B and D.** After 3 weeks of treatment.

(1.5% *Carica papaya* latex cream) or B (2% ketoconazole cream), followed by redness or erythema. Erythema was reported only in patients receiving Treatment A. Adverse effects for both treatments are comparable statistically.

No adverse effect (as defined in the Advent Event Grading scale) was reported or observed among the patients in both groups in the study. The adverse events (pruritus and erythema) reported in the first two weeks are considered as minor only, spontaneously resolved, and caused no disruption in the patient's daily activities.

Table 7 shows the summary of the Patient's Assessment of Improvement. Chi-square test was employed to demonstrate whether the patient's assessment varies significantly. The analysis resulted into a p-value of 0.000, which means that a significant difference exists in the assessment of these patients.

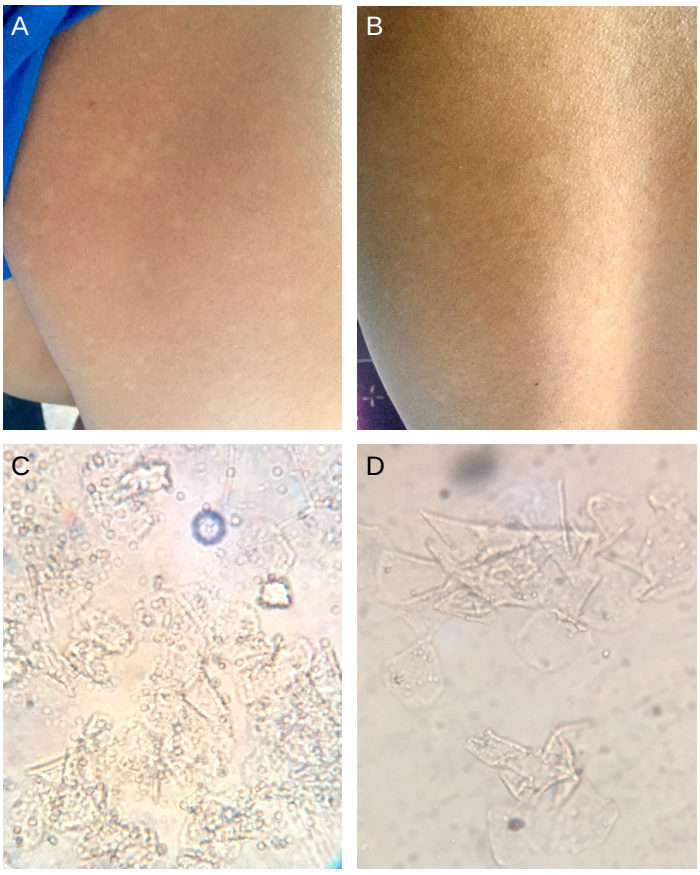

Figure 4. A and C. Representative clinical photo and KOH result of a patient treated with Treatment B (2% ketoconazole cream) at baseline. **B and D.** After 4 weeks of treatment.

Table 6. Summary of adverse effects reported by patients.

Adverse effect	Treatment A (1.5% *Carica papaya* latex cream)				Treatment B (2% ketoconazole cream)				P-value
	P*	R†	P*&R†	No AE‡	P*	R†	P*&R†	No AE‡	
Week 1	2	1	2	25	5	0	0	29	0.709
Week 2	2	0	0	28	3	0	0	31	0.750
Week 3	0	0	1	29	0	0	0	34	0.287
Week 4	0	0	0	30	0	0	0	34	1.000

*P=pruritus, †R=redness, ‡AE=adverse effect

DISCUSSION

The results of the study support the use of 1.5% *Carica papaya* latex cream as an alternative treatment to the first line therapy, which is 2% ketoconazole cream, for the treatment of pityriasis versicolor. The two groups did not differ significantly in their baseline data. All subjects enrolled in the study were cured within the 4-week study period. The clinical cure rate, measured by Grading of Scaling Score, Pruritus Scale Score, as well as the mycologic cure rate measured by KOH smear Mycologic Examination Score, are comparable in both the treatment groups. The efficacy of *Carica papaya* against pityriasis versicolor proven in this study is consistent with the study done by Buensalido in 2009 where *Carica papaya* was used to successfully treat another fungal infection, tinea corporis.[10]

Although there are more side effects noted in the *Carica*

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Table 7. Summary of the patient's assessment of the improvement.

	Patient assessment		
	0 - Clear	1 – Almost clear	P-value
TREATMENT A (1.5% *Carica papaya* latex cream)	17	13	0.000
TREATMENT B (2% ketoconazole cream)	29	5	0.000

Table 8. Summary of the patient's assessment of the improvement.

	Frequency
Chi-Square	18.750a
Df	3
Asymp. Sig.	.000

a. 0 cells (0.0%) have expected frequencies less than5. The minimum expected cell frequency is 16.0.

papaya latex cream group, namely pruritus, and erythema, the adverse effects are mild, spontaneously resolving, and do not cause disruption in daily activities.

However, significantly more patients reported better overall improvement in the 2% ketoconazole group as compared to the 1.5% *Carica papaya* latex cream group as shown in their Patient's Assessment of Improvement. This is a subjective assessment of the patient at the end of the treatment. Most of the subjects who answered "almost clear" in this field reported skin discoloration as the sign that was not completely addressed by the treatment. This was not measured in this study since skin tone may take several months to return to normal, even after being treated.[4] This was reiterated to the patients who had unresolved skin pigmentary alteration after completing the study.

CONCLUSION

1.5% *Carica papaya* latex cream may prove to be a worthwhile approach to treatment of pityriasis versicolor. 1.5% *Carica papaya* latex cream and 2% ketoconazole cream showed similar clinical and mycologic cure rates in this study.

As pityriasis versicolor tends to be recurrent in many cases especially in tropical areas like the Philippines, treatment may need to be employed more than once in an affected individual as dictated by its recurrence. *Carica papaya*, which is mainly grown (>90%) and consumed in developing countries like the Philippines[1] might be a good alternative to explore as it showed similar clinical and mycologic cure rates as the current first line therapy, 2% ketoconazole cream, in this study.

However, alteration in skin color, which is an unaddressed complaint in this study, although not a parameter for cure, can be better assessed with a longer follow-up period as it takes several months to normalize.[4] It is recommended that further studies be done with a larger sample size, long term follow-up, and assessment of skin tone normalization to have more comprehensive conclusions.

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