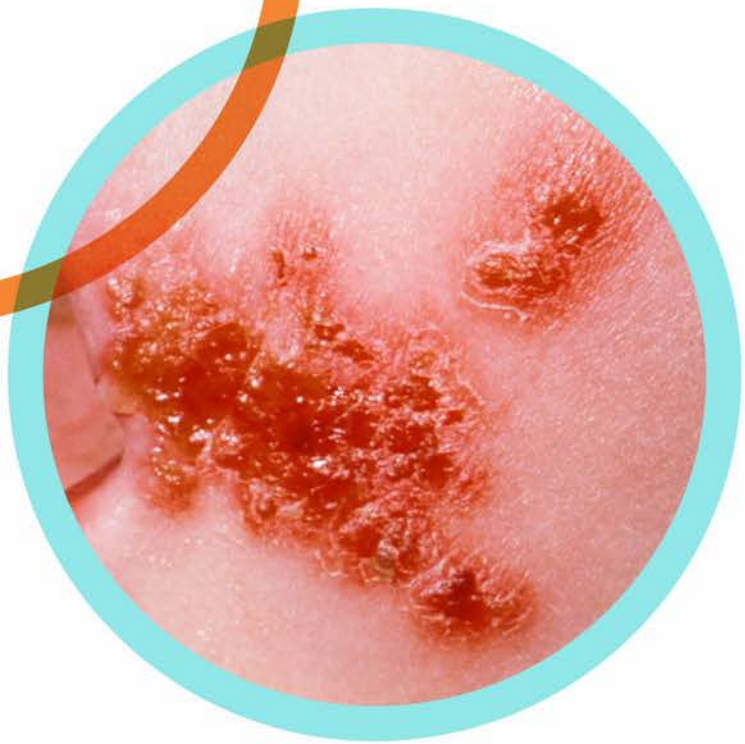

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Research Article
Efficacy of Micro-Needling with Topical Vitamin C and E Serum Versus Micro-Needling Alone in Recalcitrant Facial Melasma

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Abstract

Background and Objective: Melasma is a chronic and relapsing pigmentary skin disorder that results in symmetrical, irregular, brown macules and patches in sun-exposed areas. Despite the availability of a wide variety of therapeutic options, its treatment remains difficult as pigmentation may be recurrent. These challenges prompt the need for the appropriate management and discovering new treatment modalities. This study aims to determine the efficacy of combination treatment of micro-needling and vitamin C and E serum versus micro-needling alone in recalcitrant facial melasma. **Materials and Methods:** This is a single-blind assessor, randomized controlled clinical trial. The sample size for the study was 20. Histology samples, melasma quality of life, melasma area and severity index and clinical pictures were compared pre-and post-treatment to evaluate the result of the treatment. Mean and SD was used for melasma quality of life and melasma area and severity index. Independent sample T-test was used to compare the patients with micro-needling with vitamin C and E serum versus patients with micro-needling alone in terms of melasma quality of life and melasma area and severity index. Paired sample T-test was used to determine the significant change from pre-treatment to post-treatment of the patients. **Results:** There were better results in the micro-needling and vitamin C and E serum group versus micro-needling alone. There were no noted adverse reactions in all patients. **Conclusion:** This study can conclude that micro-needling is a safe and effective second-line treatment for facial recalcitrant melasma. The addition of vitamin C and E serum will further give better outcomes due to micro-needling transdermal drug delivery which then results in better penetration and lightening effect action.

Key words: Melasma, micro-needling, hyperpigmentation, vitamin C serum, vitamin E serum, pigmentary disorder, transdermal drug delivery

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Melasma is a chronic and relapsing pigmentary skin disorder that results in symmetrical, irregular, brown macules and patches in sun-exposed areas such as the face and less commonly, hands and forearms[1]. It generally starts at the age of 20-40 years old and is usually seen in females. It is generally a clinical diagnosis consisting of reticulated hyperpigmentation. Other useful diagnostic tools to aid in the diagnosis are dermoscopy, biopsy and ultraviolet light which will also help indicate the severity and depth of the pigmentation.

Though it is a common skin concern, its treatment remains challenging as pigmentation may be recurrent and may be recalcitrant to other treatment modalities. Because of this, melasma can be a frustrating condition not only for the patients but also for the treating physician. Hence, this study is done to research other safe and effective treatment options for melasma, especially the recalcitrant cases.

Micro-needling is a relatively new minimally invasive procedure involving controlled puncturing of the skin using miniature sterilized needles. There is minimal damage to the epidermis and because of the resulting tiny punctures and channels created, it is also now widely used as a transdermal delivery system for therapeutic drugs[2].

In a study by Lima[3], he evaluated the medical records of patients with recalcitrant melasma treated with micro-needling with needle depth of 1.5 mm. This was combined with topical depigmentation formula (0.05% tretinoin+4% hydroquinone+1% fluocinolone acetonide) after 24 hrs and in the following days. The procedure was repeated 30 days after. One hundred percent of patients reported satisfaction with the results and their study found that all patients responded to the micro-needling modality.

The effect of micro-needling in pigmentation may be due to its ability to stimulate collagen and fibroblast thereby causing improvement in the upper dermis and basal membrane which is damaged in melasma[4].

Ismail *et al.*[5] conducted a study wherein thirty female patients with melasma received six sessions of micro-needling with the addition of topical vitamin C every 2 weeks. Melasma area and severity index (MASI) score and clinical photos were used to assess the clinical improvement. They found all patients showed improvement at the end of treatment hence they concluded that micro-needling with topical vitamin C is an effective and safe treatment option for epidermal melasma, especially in Fitzpatrick skin phototypes I-III.

The depigmenting action of vitamin C is due to its action in the key steps of melanogenesis. It is a tyrosinase inhibitor thereby decreasing melanin formation. However, vitamin C is an unstable compound hence transdermal delivery using devices such as micro-needling is needed to ensure adequate delivery.

In this study, vitamin C and E are used due to their synergistic action. Vitamin E has the property of potentiating the action of vitamin C while vitamin C helps regenerate vitamin E[6,7].

To the researchers' knowledge, this is the first study investigating the effect of micro-needling with topical 15% vitamin C and 0.05% E in the treatment of recalcitrant melasma in Filipino patients.

This study aims to determine the efficacy of combination treatment of micro-needling and vitamin C and E serum versus micro-needling alone in recalcitrant facial melasma in Filipino patients.

The specific objectives are to determine if the addition of vitamin C and E with micro-needling leads to better clinical improvement defined as a decrease in MASI score in recalcitrant facial melasma, to assess the improvement in quality of life of melasma patients using melasma quality of life post-treatment at 16th week, to assess improvement through comparison of biopsy reading of pre and post-treatment in both groups and to determine the safety of micro-needling through adverse event monitoring.

MATERIALS AND METHODS

Study area: The study was carried out at Jose R. Reyes Memorial Medical Center, Department of Dermatology Out-Patient Clinic, Manila Philippines from June to November, 2019.

Study design: The researcher performed a single-blind assessor, randomized controlled clinical trial. The sample size was calculated to detect at least a 30% reduction of values of MASI scores, with an effect size (mean/standard deviation) of 1.1, alpha error of 0.05 and 80% of the power. The sample size for the study was 20 with 10 patients in each group.

Randomization was performed by keeping (n = 20) opaque envelopes in a box and patients were asked to pick one of the envelopes at the time of enrollment to determine which group they belong to.

Participants: This study included twenty Filipino men and women aged 18 and above having Fitzpatrick skin type III-VI with facial refractory melasma without specific treatment aside from sunscreen in the last 15 days. Participants were patients seen at the Jose R. Reyes Memorial Medical Center Department of Dermatology Out-Patient Clinic with refractory

melasma defined as more than 5 years of the pigmentary disorder and relapsing to more than three attempts to treatment with the first line topical triple combination of topical hydroquinone+steroid+tretinoin. Diagnosis of melasma was done through clinical examination, dermoscopy, UV light from A-One Smart skin analyzer (MEDEV Medical Devices Corporation) and 3 mm skin punch biopsy. Participants were willing to withhold additional aesthetic therapies to the proposed treatment area during the study period, able to follow study instructions and to complete all required visits and signed an IRB-approved informed consent form, photographic release form and authorization for use and release of information before any study-related procedures being performed.

Exclusion criteria were as follows:

- Facial surgery $\leq$6 months before study enrollment or plans for facial surgery during the study
- Bleeding disorders
- Presence of hypertrophic scars or keloid
- Any other facial pigmentation aside from melasma
- Recent or current history of inflammatory skin disease, infectious diseases, cancerous/pre-cancerous lesion, unhealed wound or acne in the treatment areas
- Known hypersensitivity or previous allergic reaction to any components of the micro-needling device including EMLA
- Pregnant, breast-feeding
- Patients currently on oral contraceptive pills or hormonal therapy

Treatment protocol: After randomization, patients were divided into two groups. Both groups underwent a 3 mm skin punch biopsy before the start of the first treatment and a month after the last treatment to determine the histological improvement. The histologic sections were stained with hematoxylin and eosin (H&E).

The procedure was performed under topical anaesthesia containing a eutectic mixture of lidocaine and prilocaine for 45 min. Dermapen Ultima A6 with 12 pins/needles (a micro-needling device) set on low-speed mode (412 cycles min^{-1}) in a vibrating stamp-like manner was used. This made use of disposable needles.

After preparation of the area with antiseptic and saline, the skin was gently stretched with one hand while simultaneously lowering the micro-needling device perpendicular to the skin with the other hand assisting the smooth delivery of microneedles into the skin. The treatment technique involved a combination of horizontal, vertical and oblique devices passes over the treatment areas, repeating five times. The depth of needles used depends on the site treated following the micro-needling guidelines.

Group 1 received four sessions of micro-needling in combination with topical 15% vitamin C (L-ascorbic acid) and 0.05% E serum (Lab46 SkinCare). The topical vitamin C and E serum were placed on an opaque bottle with a dropper. One drop of topical 15% vitamin C and 0.05% E serum was spread on each of the micro-needling post-treatment areas. Persistent bleeding areas were wiped with gauze wet with saline and an ice roller was used for 15 min to relieve the area.

The patients were instructed to wash the face using mild, unscented soap the next day and instructed nightly application of one drop of topical vitamin C and E serum (Lab46 SkinCare) on each of the post-treatment sites or the target sites and daily broad-spectrum sunscreen SPF 50+over the whole face and reapplied every 2 hrs while group 2 were subjected to four sessions of micro-needling alone and daily broad-spectrum sunscreen SPF 50+ over the face, with reapplication every 2 hrs and use of mild, unscented soap. The sessions were done 30 days apart.

In general, skin on the forehead, lower eyelids and nasal bridge are treated with needle depths ranging from 0.5-1.0 mm, whereas the cheeks, perioral regions and scars or striae in various body parts are typically treated with needle depths 1.5-3.0 mm. As a general rule of thumb, thicker or more brotic skin can be treated with deeper needle depths.

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Subjects returned to the clinic 2 weeks after every procedure for monitoring of side effects and week 4, 8, 12 and 16 for evaluation and additional sessions of micro-needling treatment. Any adverse effects like erythema, pruritus, infection, etc were recorded and treated accordingly. Patients will be followed-up every month for three months for any recurrence.

Data collection

Clinical assessment: The main outcome measures were a decrease in MASI scoring. The secondary outcome in clinical improvement was evaluated through photographs done by one person at baseline, 4th, 8th, 12th and 16th weeks using A one smart skin analyzer (MEDEV Medical Devices Corporation) with the same setting throughout. For assessment of response to treatment, an independent senior dermatology resident of Jose R. Reyes Memorial Medical Center (evaluator-blinded) evaluated the photographs and MASI scores at pre and post-treatment. The assessor was instructed on how to score the MASI. Scoring of MASI was based on the study of Pandya *et al*.[8] regarding reliability and assessment of MASI. The melasma score calculator app was used to input and compute the melasma area and severity index scores.

For the degree of satisfaction, the patients were asked to answer the melasma quality of life scoring at the end of treatment and were compared to their score pre-treatment. The melasma quality of life questionnaire was translated into Filipino and was validated. Pre and post-treatment (one month after the last session) biopsy readings were compared to evaluate the improvement.

Statistical analysis: Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for demographic and clinical profile variables while mean and SD was used for melasma quality of life and melasma area and severity index. Independent sample T-test was used to compare the patients with micro-needling with vitamin C and E serum versus patients with micro-needling alone in terms of melasma quality of life and melasma area and severity index during pre-treatment and post-treatment. Paired sample T-test was used to determine the significant change from pre-treatment to post-treatment of the patients. All statistical tests were two-tailed tests. Shapiro-Wilk was used to test the normality of the continuous variables. Missing variables were neither replaced nor estimated. Null hypotheses were rejected at 0.05α-level of significance. The STATA 13.1 was used for data analysis.

RESULTS

Clinical features: Table 1 shows the demographic and clinical profile of the patients enrolled in this study. It included twenty patients: 20 (100%) females, mostly in the age group >50 years old (75%) with a mean age of 56, all Fitzpatrick skin type IV, melasma duration of 5-10 years (85%), with a family history of melasma (55%), sun exposure as the predisposing factor (45%), with mostly malar distribution (80%).

Table 1: Demographic and clinical profile of the patients (n = 20)

	Frequency (%)
Age	
18-30	0
31-40	1 (5)
41-50	4 (20)
>50	15 (75)
Sex	
Male	0 (0)
Female	20 (100)
Occupation	
None	16 (80)
Government employee	1 (5)
Private employee	0
Others	3 (15)
Family history of melasma	
With family history	11 (55)
Without family history	9 (45)
Predisposing factors	
Sun exposure alone	9 (45)
Sun exposure and pregnancy	5 (25)
Sun exposure and OCP	2 (10)
Sun exposure, pregnancy and OCP	2 (10)
Pregnancy	1 (5)
Oral contraceptive pills	1 (5)
Melasma type	
Epidermal	1 (5)
Dermal	0 (0)
Mixed	19 (95)
Area affected	
Malar, Central Malar	16 (80)
Malar, Mandibular (Jawline, chin)	3 (15)
Central (forehead, nose, upper lip, chin)	1 (5)
Fitzpatrick type	
III	0 (0)
IV	20 (100)
Time of onset of melasma (years)	
5-10	17 (85)
>10	3 (15)

Diagnostic tools: Dermoscopy is a useful non-invasive tool to aid in the diagnosis of melasma. As shown in Fig. 1a and b, dermoscopy in melasma shows a brown reticular network with dark fine granules scattered on the surface in epidermal type while in dermal type, there is uniform involvement, dark brown to grey hyperpigmented lesions with reticulo globular pattern, telangiectasia and arciform structures. In the mixed type, there are features of both epidermal and dermal patterns.

Ultraviolet light from a-one smart skin analyzer (MEDEV Medical Devices Corporation) was used in the diagnosis and classification of melasma as the accentuation of pigment correlates to epidermal melasma, no accentuation in dermal type, while there is the enhancement in colour contrast in some areas while there are none in others in the mixed type.

Figure 2 shows the pre-treatment 3mm skin punch biopsy revealing increased epidermal melanocytes and the presence of dermal melanophages.

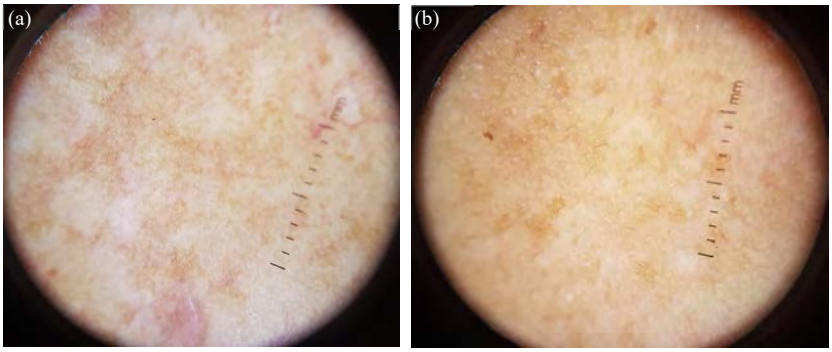

Fig. 1(a-b): Dermoscopic findings of melasma, (a) Dermoscopic findings of mixed type melasma showing the dark and light brown reticular network, telangiectasia and arciform structures and (b) More prominent dark and light brown reticular network with reticulonodular pattern and telangiectasia from a different patient with mixed type melasma

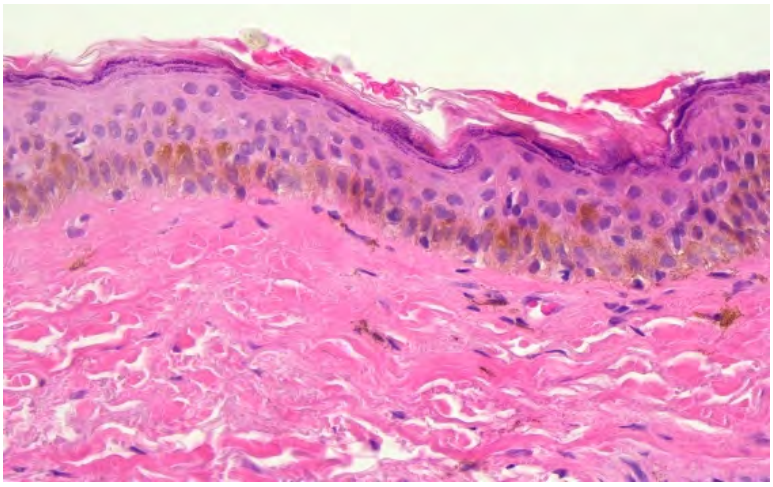

Fig. 2: High magnification view shows the increase in epidermal melanocytes, basement membrane disruption and dermal melanophages

Table 2: Clinical and quality of life measures of melasma before and after four sessions of micro-needling (n = 20)

	Mean+SD			
	Change	Pre-treatment	Post-treatment	p-value
Melasma quality of life	8.35±5.29	57.10±6.46	48.75±7.35	<0.001
Micro-needling with vitamin C and E serum	11.90±5.43	59.30±6.27	47.40±7.95	<0.001
Micro-needling alone	4.80±1.32	54.90±6.17	50.10±6.85	<0.001
Melasma area and severity index	2.67±1.51	7.59±3	4.92±2.47	<0.001
Micro-needling with vitamin C and E serum	3.59±1.54	8.24±2.86	4.65±2.29	<0.001
Micro-needling alone	1.75±0.76	6.94±3.14	5.19±2.74	<0.001

Based on these tools, the majority of our patients were classified as a mixed type of melasma (95%).

The melasma quality of life scores before and after treatment are shown in Table 2. Comparing the melasma quality of life, there is improvement in the quality of life as shown by a significant decrease in the score on overall population as well as in both groups from pre-treatment to post-treatment. The mean change of melasma quality of life overall was 8.35 from pre to post-treatment but the group with vitamin C and E serum (11.9+5.43) had the higher decrease of MelasQoL score compared with the micro-needling group alone (4.8+1.32).

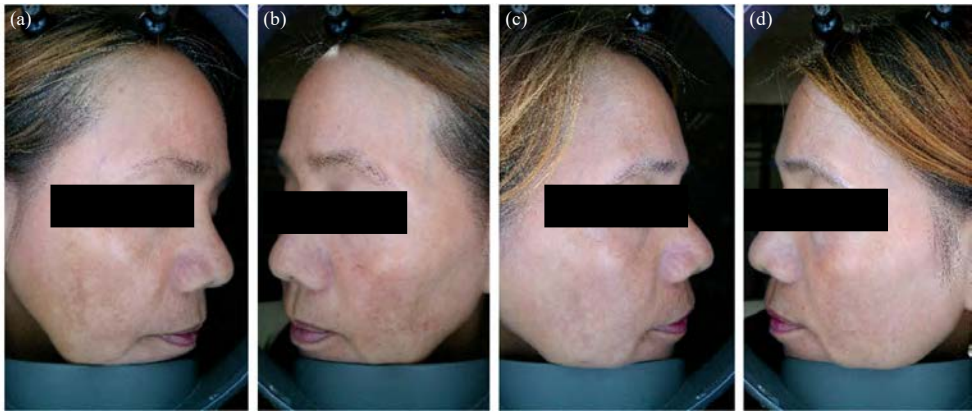

Fig. 3(a-d): Sample group 1 patient who underwent micro-needling with vitamin C and E serum, (a-b) Before micro-needling and vitamin C and E of malar and mandibular and (c-d) Decrease in hyperpigmentation of malar and mandibular after four sessions of micro-needling with vitamin C and E

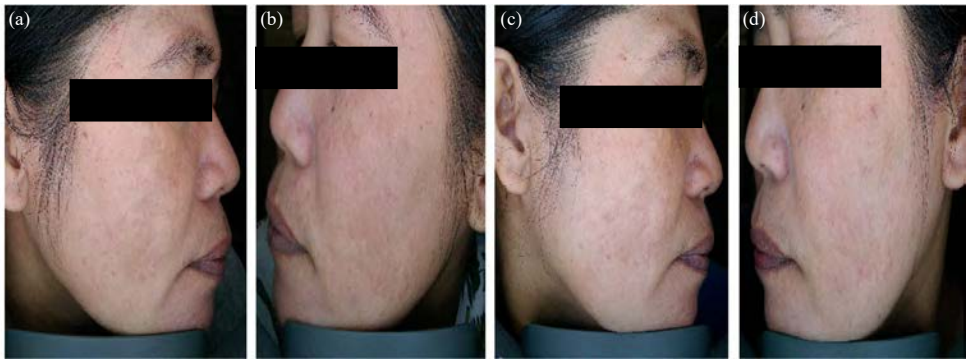

Fig. 4(a-d): Sample group 2 patients who underwent micro-needling alone, (a-b) Before micro-needling procedure alone of malar and mandibular and (c-d) Decrease in hyperpigmentation of malar and mandibular after four sessions of micro-needling

In terms of the melasma area and severity index (MASI), there is a significant decrease of the score on the overall population as well as in both groups from pre-treatment to post-treatment. The mean change of melasma area and severity index overall was 2.67 from pre to post-treatment but the group with vitamin C and E serum (3.59+1.54) had the higher decrease of melasma area and severity index compared with the Micro-needling group alone (1.75+0.76). The decreases in scores of melasma quality of life and melasma area and severity index are found to be significant ($p<0.05$).

Table 3 shows the pre-and post-treatment melasma area and severity index scores by the blinded evaluator. In terms of adverse events, all patients tolerated the procedure. They reported erythema, minimal pruritus and stinging sensation immediately after the procedure that lasted for an average of 3 days. By the time of follow-up assessment every 2 weeks post-procedure, the erythema, pruritus and stinging sensation were resolved. For group 1, they experienced transient mild stinging sensation after application of 15% vitamin C and 0.05% E serum (Lab46 Skincare) post-micro-needling procedure. There was no recurrence on reapplication of the serum in the next days.

Figure 3a-d showed the clinical results of group 1 patients (micro-needling with serum).

Figure 4a-d showed the clinical results of group 2 patients (micro-needling alone).

In both groups, there was noted clinical improvement in terms of the decrease in pigmentation as seen in these representative photographs of baseline and 12th week. Most patients also noted improvement in skin texture after the procedure.

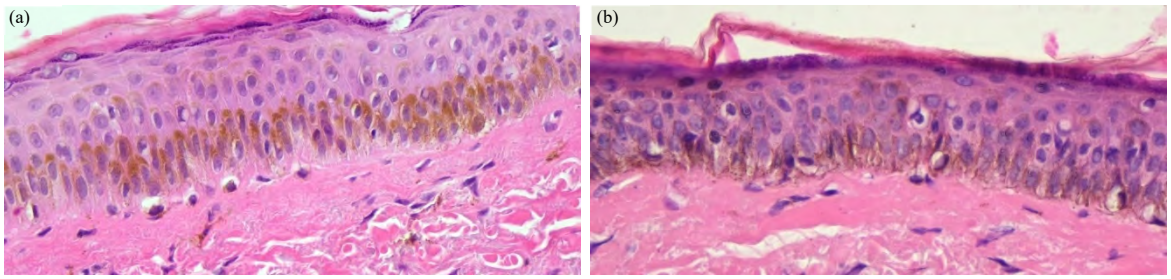

Fig. 5(a-b): Microscopic low power views of melasma skin biopsy sample in group 1, (a) Pre-treatment biopsy and (b) Post-treatment biopsy of micro-needling alone showed a decrease in epidermal melanin density

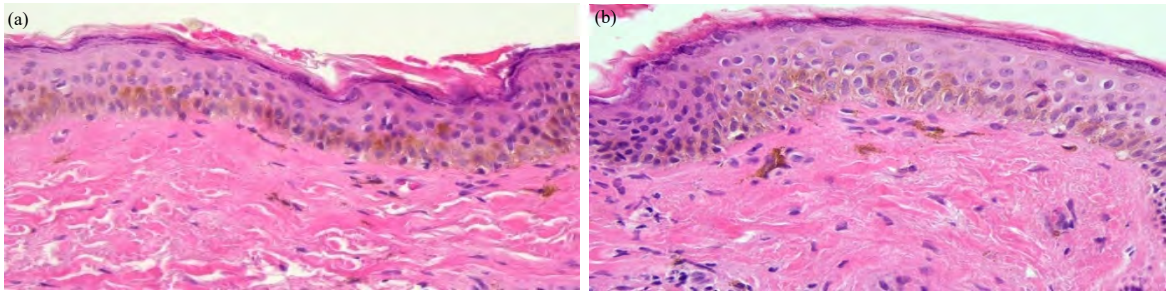

Fig. 6(a-b): Microscopic low power views of melasma skin biopsy sample in group 2, (a) Pre-treatment biopsy and (b) Post-treatment biopsy of micro-needling and topical vitamin C and E serum showed a decrease in epidermal melanin density

Table 3: Pre and post-treatment melasma area and severity index scores by the blinded evaluator

Group 1 (Micro-needling with vitamin C and E serum)		Group 2 (Micro-needling alone)	
Score pre-treatment	Score post-treatment	Score pre-treatment	Score post-treatment
4.8	1.2	3.6	1.8
6.1	3.6	10.8	7.2
6	4.1	3.6	1.8
10.8	7.2	4.8	3.6
11	5.0	4.8	3.6
4.8	1.2	6.0	5.1
6.1	3.6	11.0	9.0
10.8	7.2	11.0	9.0
11	7.4	4.8	3.6
11	5.0	9.0	7.2

Figure 5 and 6 showed the pre and post-treatment biopsy comparison of patients. Figure 5a-b showed representative biopsy thirty days after the micro-needling alone procedure.

Figure 6a and b showed pre-and post-treatment representative biopsy thirty days after the micro-needling and topical vitamin C and E serum procedure.

The biopsy result of micro-needling with vitamin C and E serum (group 2) showed that there is a more noticeable decrease in epidermal melanin density than that of the micro-needling procedure alone.

DISCUSSION

The patients enrolled in this study represent the first patients treated with micro-needling and topical 15% vitamin C and 0.05% E serum versus micro-needling alone in the Philippines. Due to Filipino skin type and higher exposure to sunlight because of the country's topographical location, Filipinos are prone to have melasma. In this current study, subjects are all women and of skin type IV, with the primary triggers of sun exposure and pregnancy, which are similar to

the epidemiology of melasma worldwide. Its course and the resulting cosmetic disfigurement harm the patient's quality of life prompting the need for the appropriate management and discovering new treatment modalities. However, its management remains challenging despite the availability of topical whitening agents and several procedures like chemical peels, lights, lasers and micro-needling to which only a few studies have been done.

Among the depigmenting agents, the most effective first-line treatment is the triple combination regimen composed of hydroquinone 4%, tretinoin 0.05% and fluocinolone acetonide 0.01% and photoprotection including sunscreen[9]. However, this topical therapy is to be used for a maximum of three months after which it should be stopped or the dose should be gradually reduced and replaced with a safer treatment maintenance therapy to avoid its side effects. Procedural therapeutic options are also available and used alone but most commonly as an adjunct to the topical first-line treatment for recalcitrant melasma. These procedures are done with precaution because of the risk of post-inflammatory hyperpigmentation and are often ineffective with the unpredictable response, especially in those with darker skin. Few studies were done on the relatively new minimally invasive procedure of micro-needling and it was proven to be safe, highly efficacious and is a viable option for the skin of colour[10].

But as with the previous researchers, the exact mechanism of action of micro-needling in melasma in this study is still unknown but improvement of patients may be attributed to modifications that occurred in the skin after moderate injury. The needles penetrate the stratum corneum and create micro-channels with minimal damage to the epidermis leading to collagen and elastin production. As stated by Kaur *et al.*[2] and the study of Singh *et al.*[11] micro-needling can stimulate fibroblast and collagen production resulting in improvement of papillary dermis and restoration of basement membrane in melasma.

In this pre and post-biopsy specimens, improvement was seen as there was a decrease in epidermal melanin, basement membrane disruption and decrease in dermal melanophages similar to previous studies. Histological improvements were also more pronounced in the micro-needling and vitamin C and E serum groups.

As for the application of vitamin C and E serum, it resulted in better improvement since the serum acts synergistically to interrupt the important pathogenesis of melanin production. Vitamin C inhibits the action of tyrosinase, thereby decreasing melanin formation[12]. While the antioxidant vitamin E potentiates the action of vitamin C four-fold thereby increasing its efficiency. In addition, this skin lightening may also be due to enhanced transdermal delivery system after micro-needling leading to enhanced drug absorption and uniform administration of the drug[13].

Several scoring and evaluation tools were developed to assess the efficacy of melasma treatments. One of which is the melasma area and severity index (MASI) which is a valid scale used to score the extent or severity of hyperpigmentation in melasma. Since melasma has a significant impact on appearance, it can cause psychological and emotional distress to patients causing a reduction in their quality of life hence it is important to evaluate and consider the melasma quality of life in the treatment approach. In this study, there was noted improvement in the quality of life meaning a better sense of well-being of the patients after the treatment. Clinical evaluation was also done through melasma area and severity index score conducted by a dermatologist.

There was a significant difference in the MASI score and Melasma quality of life after micro-needling with and without vitamin C and E serum. These results were comparable with the previous studies done by other researchers. There was also clinical improvement as seen in pre-and post-treatment photographs. In the present work and previous studies of Lima[3], Ismail *et al.*[5], Cohen *et al.*[10], Singh *et al.*[11], micro-needling was found to be effective in the treatment of melasma as measured in MASI and MELASQoL. However, there was a noticeable decrease in MASI score in the micro-needling with vitamin C and E group attributed to the benefit of depigmenting action of vitamin C and E. This agrees with Ismail *et al.*[5], Matsuda *et al.*[6], Inui *et al.*[12], Telang[7] who noted the benefits of vitamin C in the treatment of pigmentary concerns such as melasma.

The participants and primary investigator were not blinded to the study treatment. Moreover, a comparative analysis of the relation of the demographic profile of a patient with improvement was not determined. Recurrence rates were not measured in this study.

Since the exact mechanism of action of micro-needling is not yet well established, further studies are needed. Further randomized controlled studies are needed to compare the efficacy of micro-needling with vitamin C and E serum with other melasma therapeutic options. The researcher also recommends the use of dermoscopy before and after treatment as one of the determinants of clinical improvement. Long-term follow-up is needed to evaluate for any recurrence and the safety of vitamin C and E serum as maintenance therapy.

CONCLUSION

Both micro-needling and a combination of micro-needling with vitamin C and E serum are effective treatment modalities for recalcitrant melasma. However, the combination of micro-needling and vitamin C and E serum showed better results in terms of observed clinical skin lightening and patient's quality of life score. Better improvement was also seen histologically as observed in the decrease in epidermal melanin density in the micro-needling with vitamin C and E serum group attributed to enhanced drug delivery and its lightning action. Therefore, this study can conclude that a combination of micro-needling and vitamin C and E serum is a safe and effective second-line treatment for patients with recalcitrant facial melasma having skin type IV. There were no noted adverse events hence this will provide confidence to the physicians in doing this type of procedure. Patients were also satisfied with the treatment with reported improvement in their quality of life which is an important aspect in melasma management.

SIGNIFICANCE STATEMENT

This study provides further evidence regarding the safety and efficacy of micro-needling in the treatment of facial recalcitrant melasma in patients with darker skin types without the concern for lasting post-inflammatory hyperpigmentation. This will offer an effective option for patients who have already undergone the first-line topical treatment and certain procedures such as lasers and chemical peels or who are contraindicated to undergo the said treatments. This study also discovers the additional benefit of vitamin C and E serum as a depigmenting agent in combination with the action of micro-needling modality. This can be a safe option for patients who have already reached the maximum length of treatment for the triple combination therapy or who are contraindicated to receive such topical treatment.

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REFERENCES

1. Ogbechie-Godec, O.A. and N. Elbuluk, 2017. Melasma: An up-to-date comprehensive review. Dermatol. Ther., 7: 305-318.
2. Kaur, A. and M. Bhalla, 2019. Topical tranexamic acid with microneedling in melasma. Acta Sci. Med. Sci., 3: 124-126.
3. de Andrade Lima, E., 2015. Microneedling in facial recalcitrant melasma: Report of a series of 22 cases. An. Bras. Dermatol., 90: 919-921.
4. Iriarte, C., O. Awosika, M. Rengifo-Pardo and A. Ehrlich, 2017. Review of applications of microneedling in dermatology. Clin. Cosmet. Invest. Dermatol., 10: 289-298.
5. Ismail, E.S.A., A. Patsatsi, W.M.A. El Maged and E.E.A.E. Nada, 2019. Efficacy of microneedling with topical vitamin C in the treatment of melasma. J. Cosmet. Dermatol., 18: 1342-1347.
6. Matsuda, S., H. Shibayama, M. Hisama, M. Ohtsuki and M. Iwaki, 2008. Inhibitory effects of a novel ascorbic derivative, disodium isostearyl 2-o-l-ascorbyl phosphate on melanogenesis. Chem. Pharm. Bull., 56: 292-297.
7. Telang, P.S., 2013. Vitamin C in dermatology. Indian Dermatol. Online J., 4: 143-146.
8. Pandya, A.G., L.S. Hynan, R. Bhore, F.C. Riley and I.L. Guevara *et al*., 2011. Reliability assessment and validation of the melasma area and severity index (MASI) and a new modified masi scoring method. J. Am. Acad. Dermatol., 64: 78-83.E2.
9. Shankar, K., K. Godse, S. Aurangabadkar, K. Lahiri and V. Mysore *et al*., 2014. Evidence-based treatment for melasma: Expert opinion and a review. Dermatol. Ther., 4: 165-186.
10. Cohen, B.E. and N. Elbuluk, 2016. Microneedling in skin of color: A review of uses and efficacy. J. Am. Acad. Dermatol., 74: 348-355.
11. Singh, A. and S. Yadav, 2016. Microneedling: Advances and widening horizons. Indian Dermatol. Online J., 7: 244-254.
12. Inui, S. and S. Itami, 2007. Perifollicular pigmentation is the first target for topical vitamin C derivative ascorbyl 2-phosphate 6-palmitate (APPS): Randomized, single-blinded, placebo-controlled study. J. Dermatol., 34: 221-223.
13. Fabbrocini, G., V. de Vita, N. Fardella, F. Pastore and M.C. Annunziata *et al*., 2011. Skin needling to enhance depigmenting serum penetration in the treatment of melasma. Plast. Surg. Int., Vol. 2011. 10.1155/2011/158241.