The Effectiveness of a 650 µm Microneedle Patch for the Improvement of Nasolabial Folds: A Pre-Post Study

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Abstract

In dermatology, the pursuit of youthful skin is increasing in popularity, with both invasive and non-invasive methods available for skin rejuvenation. Microneedling has become a standout, non-invasive technique for improving skin texture and appearance. Although there is extensive research on the safety and effectiveness of needle depth, the ideal depth for treating nasolabial folds remains unclear. This study aimed to examine the impact of a 650 µm microneedle patch on nasolabial fold improvement in 36 female participants with varying severities of nasolabial folds according to the Merz Aesthetic scale. The outcomes of treatment were evaluated by independent dermatologists who reviewed wrinkle grades according to the Merz aesthetics scale by using digital photographs. Wrinkle size was evaluated by using ANTERA 3D at baseline and during follow-up at 4, 8, and 12 weeks. Over 12 weeks, using 650 µm microneedle patches resulted in significant improvements in the nasolabial fold area, as assessed by dermatologists and patient satisfaction surveys, without serious side effects. This indicates the effectiveness of 650 µm microneedle patches in enhancing the nasolabial fold area.

Keywords: *Rejuvenation, Youthful Appearance, Microneedle, Nasolabial Fold*

1. Introduction

Skin rejuvenation focuses on treatments to revive and maintain a youthful skin appearance. In recent years, advancements in dermatology and cosmetology have introduced new rejuvenation methods. As technology advances, new methods have emerged to effectively and efficiently address these concerns. Among these, microneedle patches have gained attention for their non-invasive nature and effectiveness in improving skin appearance.

Microneedle therapy has been used to treat a variety of medical issues, including skin rejuvenation, by the mechanism of percutaneous collagen production through an inflammatory response, improving skin texture, and aiding in drug delivery (Jin et al., 2009).

Regarding the mechanism of drug delivery, the combined use of a soluble microneedle patch and wrinkle cream has been demonstrated to effectively reduce facial wrinkles and enhance skin rejuvenation (Hong et al., 2017). Furthermore, it is utilized not only as a transdermal delivery system due to the occurrence of micro-injuries but also as a collagen induction therapy. According to a previous split-face study, Thai females between 30 and 60 years old with mild to moderate nasolabial folds according to the Merz aesthetic scale found that applying a microneedle patch, both with and without an active ingredient, and a microneedle

patch alone with a needle-length of 1100 μm microneedles effectively reduced facial wrinkles, particularly in the nasolabial folds (Pruettijarai et al., 2022).

The objective of this study is to assess the effectiveness and safety of using a shorter microneedle patch alone for rejuvenating nasolabial folds, employing a pre-post-study approach with 650 μm microneedles. The evaluation process will be conducted every 4 weeks over a total of 12 weeks of sessions. To evaluate the effectiveness for each participant, both subjective and objective evaluations will be used.

2. Objectives

To evaluate the efficacy of a microneedle patch for the improvement of nasolabial folds.

3. Materials and Methods

The research employed a pre-post study design conducted from June to August 2023 at the Department of Dermatology, Benchakitti Park Hospital and Thammasat University Hospital, Thailand. Approval for all study protocols, along with supporting data, was granted by the Institutional Review Board of the Human Research Ethics Committee of Thammasat University (Medicine) under reference number MTU-EC-OO-0078/64 on November 25, 2021.

3.1 Patient selection

The study included 36 female volunteers aged 25 to 60 years old with mild to severe nasolabial folds according to the Merz Aesthetics Scale. Participants with the following conditions were excluded from the study:

1. Pregnancy or breastfeeding
2. Current or previous history of active skin diseases
3. Uncontrollable systemic diseases
4. History of immunosuppressive therapy administration
5. History of taking antiplatelet or anticoagulant medication within the last month
6. Botox and/or filler injections received at the nasolabial folds within the previous year
7. Energy-based device and/or laser therapy received within the previous year
8. Allergy or hypersensitivity to polymethylmethacrylate (PMMA) and monomer plastics

3.2 Study methods

The microneedle (MN) array was fabricated by the Nanoneedle Research Team (NND), Responsive Material and Nanosensor Research Group (RMNS), National Nanotechnology Center (NANOTEC), Thailand. Conformity was declared by the European Committee. The microneedle array was fabricated on a fabric substrate via the photo-polymerization technique. Each microneedle was designed with a pyramidal shape.

In this study, the average height (h) of the microneedles was 650 μm, with a density of 120 needles/cm². The base diameter (w) measured 370 μm, and the distance between the tips of the microneedles (d) was 1,288 μm. A skin irritation test was performed on the patient five minutes before the treatment session, and the subject's skin irritation was evaluated visually an hour after the patch was removed. Subjects applied the MN for 5 minutes nightly, after washing their faces with cleanser, twice a week for a total of 12 weeks. The study participants were not allowed to use any other products during the treatment session. The evaluation of outcomes was conducted during follow-up periods at 4, 8, and 12 weeks.

3.3 Assessment

3.3.1 Subjective assessment

Digital photography was evaluated at baseline (before treatment) and following the treatment session at 4, 8, and 12 weeks. All digital photographs of the subjects' faces were taken at a straight angle and 45° using a Canon DSLR 100D.

Two dermatologists independently evaluated wrinkle grade according to the Merz aesthetics scale as 0 = No folds, 1 = Mild folds, 2 = Moderate folds, 3 = Severe folds, and 4 = Very severe folds by examining photographs that were taken at baseline and each follow-up.

The participants were also asked to evaluate the degree of improvement of facial wrinkles as Excellent (4) > 75%, Good (3) = 51-75%, Fair (2) = 25-50%, Slightly better (1) < 25 %, and Worse (0) = Clinically worse for any percentages.

Any possible side effect was monitored and assessed during each follow-up period, encompassing evaluations for pain score, itching, erythema, and scaling.

3.3.2 Objective assessment

Skin roughness and wrinkles were measured by Antera 3D.

3.4 Data analysis

All data are presented as means. In all cases, a p-value < 0.05 will be considered statistically significant. All statistical analyses will be performed using SPSS. A generalized estimating equation (GEE) was used for statistical analysis before and after comparisons within the group.

4. Results

4.1 Study population

A total of thirty-six females participated in the study. The participants' ages ranged from 25 to 59 years, with an average age of 34.25 ± 8.07 years. All participants had healthy skin (Table 1), and none of the participants had any history of allergies to polymethylmethacrylate (PMMA).

Table 1 Baseline Demographic data

	Statistic data	
	n	**%**
Female	36	100
Age (mean ±SD)	34.25 ± 8.07 [25-59]	
Skin type		
Normal skin	36	100

4.2 Efficacy

The mean grading of the Merz Aesthetic Scale in the nasolabial fold area was 1.74± 0.7 at baseline treatment. At Week 12, the mean severity grade was 1.51 ± 0.79, which was statistically significant, with a p-value of 0.002. There was a statistically significant improvement in the grading severity of the nasolabial fold after 12 weeks compared to the baseline (Table 2 and Figure 1).

Table 2 The mean grading severity at baseline, 4th, 8th, and 12 weeks

Grading severity from baseline	**Nasolabial fold (650 µm microneedle patch)**		
	Mean ± SD.	**Mean change (95% CI)**	***p*-value**
Week 0	1.74 ± 0.7	Reference	1
Week 4	1.97 ± 0.7	0.24 (0.1, 0.38)	0.001*
Week 8	1.68 ± 0.67	-0.06 (-0.2, 0.08)	0.435
Week 12	1.51 ± 0.79	-0.22 (-0.36, -0.08)	0.002*

The mean wrinkle size measured by Antera 3D in the nasolabial fold area was 10.58± 4.5 at baseline treatment. At Week 12, the mean wrinkle size was 10.27 ± 3.6. There was no statistically significant improvement in the wrinkle size measured by Antera 3D after 12 weeks compared to the baseline (Table 3).

Table 3 The mean wrinkle size by ANTERA 3D at baseline, 4th, 8th, and 12 weeks

Wrinkle size	Nasolabial fold (650 µm microneedle patch)		
	Mean ± SD.	**Mean change (95% CI)**	***p*-value**
Week 0	10.58 ± 4.5	Reference	1
Week 4	10.85 ± 3.64	0.28 (-0.87, 1.42)	0.635
Week 8	10.58 ± 4.66	0 (-1.14, 1.15)	0.996
Week 12	10.27 ± 3.6	-0.2 (-1.35, 0.96)	0.738

Throughout the treatment period, patient satisfaction with the improvement of nasolabial fold wrinkles was assessed at each follow-up. The average satisfaction score indicating the degree of wrinkle improvement steadily increased from 2.52 at week 4, a 25-50% improvement, to 3.08 at week 12, which corresponds to an improvement of 51-75%. There was a statistically significant improvement in the wrinkle size of the nasolabial fold after 12 weeks compared to the baseline (Table 4).

Table 4 Patient satisfaction

Patient Satisfaction	Mean ± SD.	*p*-value
Weeks 4	2.53 ± 0.94	
Weeks 8	2.89 ± 0.67	
Weeks 12	3.08 ± 0.55	0.001*

4.3 Adverse effects

Mild erythema was reported by 80% of participants immediately following the application of the microneedle patch, with recovery times ranging from 0 to 3 minutes. The pain level, as measured on a visual analog scale, ranged between 2 and 3. There were no reports of any serious adverse effects.

5. Discussion

The current study investigated the effectiveness of a microneedle patch with reduced length for improving the appearance of nasolabial folds. The study was designed to utilize a pre-post-study approach. The selection criteria were specific, targeting female participants aged 25 to 60 with mild to severe nasolabial folds, excluding those with various medical conditions and recent treatments that could affect skin conditions and collagen production.

The results show that there was a statistically significant improvement in the Merz Aesthetic scores for nasolabial folds as evaluated by individual dermatologists using digital photography with a patch measuring 650 µm in length and a density of 120 needles/cm^2. The satisfaction scores also showed statistically significant improvement. However, the mean wrinkle size measured by Antera 3D showed a slight

improvement with no statistically significant change. This lack of significant change can be attributed to the characteristics of the nasolabial fold, which is a deeper wrinkle that often undergoes movement during activities such as chewing and speaking. The assessment of wrinkle grading scores and wrinkle sizes showed improvement post-treatment compared to baseline. However, there was a slight increase in the mean score at week 4 from baseline, likely attributed to technical errors and variations in lighting conditions and photographic settings during the assessment with photographs and Antera 3D. Nevertheless, the severity of grading evaluated by dermatologists and wrinkle sizes measured by Antera 3D in the final session after the 12 weeks corresponded and demonstrated a decrease compared to assessments at both baseline and week 4.

The improvement in facial wrinkles is a result of the percutaneous collagen induction mechanism, which is initiated by the wound healing process in response to micro-injuries to the skin. Microneedle therapy is known for stimulating collagen production and enhancing skin texture.

Many previous studies investigated the efficacy of microneedle patches for drug administration and percutaneous collagen production for skin rejuvenation (Jin et al., 2009). Hong et al. (2017) demonstrated that the combination use of a soluble microneedle patch and wrinkle cream effectively reduces facial wrinkles and enhances skin rejuvenation. Furthermore, it is utilized not only as a transdermal delivery system due to the occurrence of micro-injuries but also as a collagen induction therapy. McCrudden et al. (2015) reported that microtrauma induced by microneedling devices promoted skin rejuvenation and improved skin appearance by stimulating the production and deposition of collagen. The micro-injury triggered the wound healing process; during the process, collagen type III is converted into collagen type I, which occurs as a result of neocollagenesis and neovascularization, resulting in skin tightening (Fernandes, 2002). Microneedle patches have been shown to be useful in cosmetic applications due to their safety profile and efficacy in enhancing wrinkle appearance (Kim et al., 2014; Jung et al., 2021).

Mild erythema and mild pain score levels were recorded during the treatment session. Reducing the length of the needles can also improve the appearance of nasolabial fold wrinkles without causing any serious side effects and minimizing pain levels. Skin redness following microneedle use is a result of the skin's immune response and can typically recover, restoring the skin barrier function, within hours after the device is applied (McCrudden et al., 2015).

A previous split-face design study by Pruettijarai et al. (2022) demonstrated that a Thai female with mild to moderate nasolabial folds according to the Merz aesthetic scale benefited from applying a microneedle patch, both with and without an active ingredient. The study revealed that employing a microneedle patch alone, with a needle length of 1100 μm, effectively diminished facial wrinkles in the area of the nasolabial folds. Consequently, it was found in the present study that reducing the microneedle patch depth to 650 μm microneedles also proved effective in decreasing the grading of nasolabial folds without any serious side effects.

This research intended to develop microneedle patches that are simple to use for self-application at home. This study was limited in terms of its duration; regular and long-term usage could lead to improvements in the appearance of nasolabial fold wrinkles. Further studies should focus on improving microneedle therapy methods by evaluating various needle lengths. A larger population, a longer duration, and a higher frequency for the application of microneedle patches may result in an even more significant effect on skin rejuvenation. The microneedle patch might be designed to prevent improper attachment. Also, studying needle sizes that reach the dermis with the confirmation of histology might be beneficial to determine the optimal needle depth for improving facial wrinkles.

6. Conclusion

According to this study, the effectiveness of the 650 μm microneedle patch in improving the aesthetic appearance of nasolabial folds during a 12-week treatment session, with patient satisfaction scores corroborating the objective severity grading, increased significantly. However, changes in wrinkle size did not improve statistically or significantly. No serious adverse effects were reported.

7. Acknowledgements

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