Combined use of energy-based interventions with low-dose isotretinoin for inflammatory acne: An institutional retrospective cohort analysis

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ABSTRACT

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***Background**:* The combined use of oral isotretinoin with energy-based interventions including fractional microneedle radiofrequency, pulsed dye laser, and ablative fractional laser is an effective way to treat moderate-to-severe inflammatory acne lesions. However, studies regarding its efficacy and safety are limited.

***Objective**:* This study aimed to assess the efficacy and safety of a treatment using low-dose isotretinoin with energy-based interventions for inflammatory acne.

***Methods**:* This retrospective cohort study included 126 patients who were diagnosed with inflammatory acne and were treated with systemic isotretinoin for at least 3 months. Patients were divided into EBD (energy-based intervention) (n=82) and non-EBD groups (n=44). Clinical outcomes of both groups were assessed using medical records and digital photographs.

***Results**:* After treatment, the modified Global Acne Grading Score of the EBD

and non-EBD groups decreased by 35.1±17.2 and 25.6±10.1, respectively. The improvement in acne severity was significantly greater in the EBD group than in the non-EBD group. Cumulated isotretinoin dose and frequency of drug-related side effects were significantly higher in the non-EBD group than in the EBD group.

***Limitation**:* This was a single-center retrospective study.

***Conclusion**:* Combined treatment with low-dose isotretinoin and energy-based intervention is well tolerated and associated with positive responses in patients with inflammatory acne.

Key words: inflammatory acne; oral isotretinoin; fractional microneedle radiofrequency; pulsed dye laser; ablative fractional laser

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I. INTRODUCTION

Acne vulgaris is a common skin disease that can lead to severe scarring and cosmetic disfigurement if patients receive inappropriate management.[1, 2] Administration of oral isotretinoin is widely considered as the most effective treatment of inflammatory acne; it is especially recommended for severe recalcitrant acne or moderate acne with scarring.[3, 4] However, a conventional dose regimen (1–1.5 mg/kg/d) can cause intolerable mucocutaneous side effects, especially in Asian patients. Alternatively, a low-dose regimen (0.15–0.4 mg/kg/d or 10–20 mg/d) was suggested to be well tolerated and elicit positive responses.[4, 5]

Energy-based interventions such as fractional microneedle radiofrequency (FMRF), pulsed dye laser (PDL), and fractional laser are increasingly being recognized as promising treatments for acne. Many studies have reported a considerable reduction of inflammatory acne lesions after several sessions of FMRF or PDL without any serious adverse outcomes.[6-10]

Fractional laser therapy is mainly used for treating acne scars, but it has also shown positive responses in patients with active acne lesions.[11, 12] In the past, as systemic isotretinoin treatment was believed to cause abnormal scarring and delayed wound healing, cutaneous procedures were not recommended in patients who were taking oral isotretinoin or had completed treatment within 6 months. However, recent studies have reported that oral isotretinoin intake did not interfere with the wound healing process after laser procedures.[13-15]

Therefore, the combined use of low-dose oral isotretinoin with laser or energy-based interventions could be an effective treatment for moderate-to-severe inflammatory acne lesions. To our knowledge, no study has investigated the effectiveness of the combined use of energy-based interventions with low-dose isotretinoin in the treatment of inflammatory acne, especially in the long term and in real-world practice. We performed a retrospective cohort study to assess the efficacy and safety of a treatment using low-dose isotretinoin with energy-based interventions for inflammatory acne.

II. MATERIALS AND METHODS

1. Study design and interventions

In this retrospective cohort study, we identified all patients with inflammatory acne who presented to a specialized scar laser clinic of a quaternary referral center from January 1, 2015 to March 1, 2020. Patients must have had a board-certified dermatologist-confirmed diagnosis of inflammatory acne, been prescribed low-dose isotretinoin for more than 3 months, and had 12 months of follow-up visits to be included. Patients were excluded if comorbid inflammatory skin diseases other than acne were present or if they were taking oral medications other than isotretinoin. Patients typically received isotretinoin

at a dose of 10–20 mg daily, but this could be tapered to 10 mg every 2 days based on individual adherence and tolerance to therapy.

While taking oral isotretinoin, all patients were encouraged to undergo energy-based intervention irrespective of the acne severity; thus, the decision was mainly dependent on the patient's preference, and patient allocation to EBD (energy-based intervention) or non-EBD group was considered to occur via a random-like process. Patients in the EBD group must be treated with energy-based intervention while taking systemic isotretinoin or within 1 month after completion of isotretinoin treatment. Two skilled board-certified dermatologists (J.H.L. and J.H.K.) performed energy-based intervention treatment on a regular basis during each visit; they choose PDL, FMRF, or PDL plus FMRF based on the lesion types and each patient's preference. After receiving one-pass, full-face treatment using FMRF and/or PDL, patients who had a depressed post-acne scar also underwent 10,600-nm ablative fractional carbon dioxide laser (AFL) therapy partially on the affected area.

2. Data collection and outcomes

We collected the following data: patient demographics, disease duration, total isotretinoin dose taken during the study period, and details of the therapeutic modalities including concomitant energy-device interventions (PDL, FMRF, and AFL) and topical medications.

The primary endpoint of the study was the assessment of the grade of acne severity. Two board-certified dermatologists (Y.I.L. and J.M.K.) independently assessed acne severity using the modified Global Acne Grading Score (mGAGS) based on digital photographs (Table 1).[16] The acne severity grade was assessed at the initial visit, 3±1 months after receiving treatment, and 12±2 months after receiving treatment; We referred these time points as '3 months' and '1 year' in this study, respectively. Additionally, the global improvement scale was used to

evaluate clinical improvement based on a 0–4-point scale (0=no improvement or worse; 1=1–25% improvement; 2=26–50% improvement; 3=51–75% improvement; and 4=76–100% improvement).[17]

Table 1. The modified global acne grading score.

Factor rated by Location		**Factor rated by Clinical Assessment**	
Score	**Location**	**Score**	**Clinical Assessment**
1	Chin	0	no lesion
1	Nose	1	≥1 comedone
2	Forehead	2	1 papule
2	right cheek	3	1 pustule
2	left cheek	4	1 nodule
Factor rated by number of lesions		**Local score** = L ×A × N the sum of local scores = modified global score **Severity of acne**: 0=none; 1-32=mild; 33-58=moderate; ≥59=severe	
Score	**Number of lesions**		
1	0-10 lesions		
2	11-20 lesions		
3	21-30 lesions		
4	31 lesions		

Systemic isotretinoin-related side effects including abnormalities in laboratory findings, severe dryness, headache, and gastrointestinal adverse events were recorded from medical records. Side effects related to the energy-based intervention including erythema, edema, and pigmentary change were also assessed. After 12 months of treatment, we also investigated disease relapse for each group. Relapse was defined as the recurrence of active disease 6 months or more after discontinuing oral isotretinoin therapy.

3. Statistical analysis

Clinical characteristic were compared between the two groups using a chi-square test or Fisher exact test if variables were in 2×2 categorical tables. A Mann-Whitney U test was used to compare continuous variables between the groups. Subgroup analysis was also performed in the energy-based intervention treatment group. Repeated measures analysis of variance (RM-ANOVA) was used to analyze the interaction of acne severity at all time points with time and treatment group allocation. Post-hoc analysis of each time point was conducted using an independent t-test with Bonferroni correction. To identify the effect of each variable on the clinical outcome, linear regression analysis was performed. All statistical analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA) and the differences were considered as significant differences if $P<0.05$.

III. RESULTS

1. Patient Characteristics

One hundred twenty-six Korean participants were included in the study. Patients were classified into the EBD (n=82) and non-EBD groups (n=44) (Table 2). More than half of the patients (71/126, 56.3%) had inflammatory acne for more than 3 years, although most of them had received previous treatment at primary clinics. There was no significant difference in the frequency of female sex, age at diagnosis, disease duration, and Fitzpatrick skin type between the groups. Moreover, there were no significant differences between acne severity of the groups at initial visit. Photographs of representative cases before and after treatment are shown in Figure 1a–d.

Table 2. Patient characteristics and clinical findings

Feature	EBD (n=82)	Non-EBD (n=44)	Total (n=126)	*p* value
Female gender	40 (48.8)	21 (47.7)	61 (48.4)	0.99
Age at the diagnosis, years	21.6±4.4	21.2±6.2	21.5±5.1	0.11
Disease duration (months)	51.5±45.1	36.8±29.8	46.4±40.9	0.057
Fitzpatrick skin type				
II	13(15.9)	9 (20.5)	22 (17.5)	
III	47 (57.3)	29 (65.9)	76 (60.3)	0.131‡
IV	22 (26.8)	6 (13.6)	28 (22.2)	
Initial mGAGs	49.3±20.2	48.3±13.5	49.0±18.1	0.69
Severity of acne†				
Mild	20 (24.4)	5 (11.4)	25 (19.8)	
Moderate	39 (47.6)	29 (65.9)	68 (54.0)	0.54‡
Severe	23 (28.0)	10 (22.7)	33 (26.2)	

†The modified global score determines the severity of acne: 1-32=mild; 33-58=moderate; >58=severe.

‡Linear-by-linear association test was used when variables were in ordered categorical 2x3 tables.

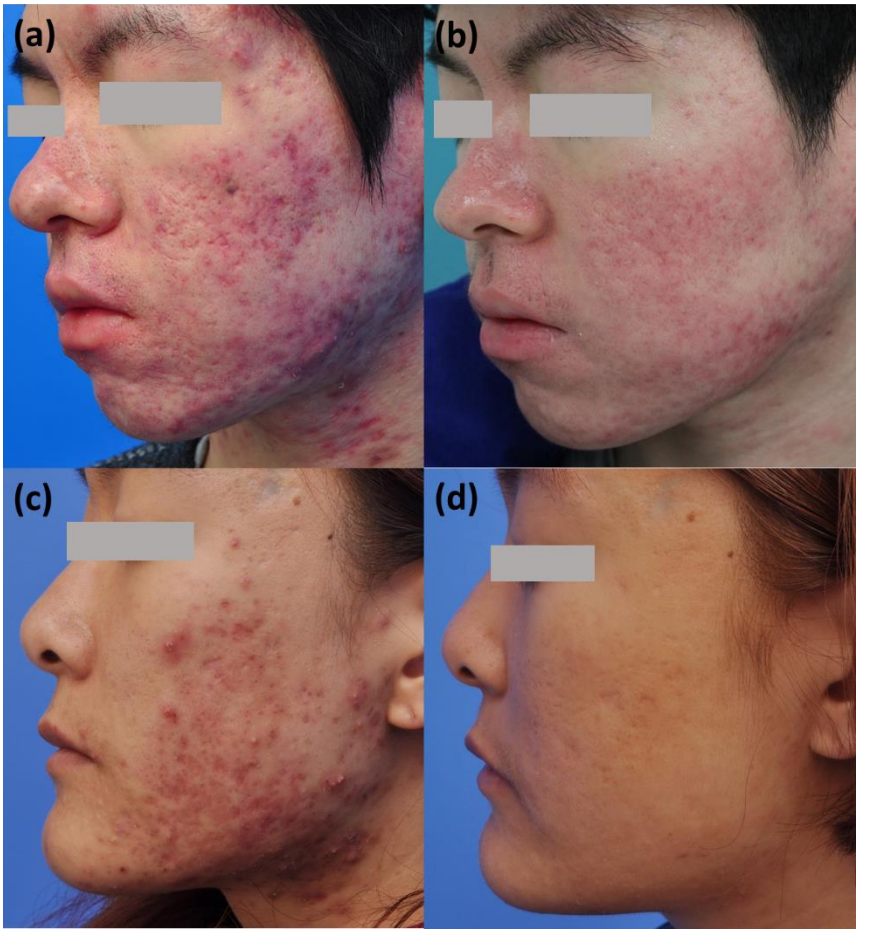

Figure 1. (a) Photographs of an 18-year-old male patient with inflammatory acne before treatment, (b) at 12 months after needle radiofrequency, pulsed dye laser, and fractional laser treatment (12 times. (c) Photographs of a 20-year-old female patient with inflammatory acne before treatment, (d) at 9 months after pulsed dye laser treatment (4 times).

2. Treatment regimens and clinical responses

In this cohort (Table 3), the mean 1-year accumulated isotretinoin dose was 3782.1±2115.9 mg. The non-EBD group was treated with a significantly higher dose of isotretinoin than the EBD group(4535.0±2350 mg versus [vs.] 3378.1±1871.4 mg, P=0.004, respectively). Most patients in the EBD group underwent treatment using FMRF+AFL (n=44, 53.7%), followed by PDL+AFL (n=24, 29.3%), and FMRF combined with PDL+AFL (n=14, 17.1%). The average number of energy-based intervention treatments during the follow-up period was 5.78±2.15. Among the local treatment regimens, topical salicylic acid (n=66, 51.6%) and intralesional triamcinolone (n=57, 45.2%) were most frequently used.

The mGAGS of the EBD group decreased from 49.3 (initial) to 28.6 (3 months) and 14.2 (1 year) while the mGAGS of non-EBD group decreased from 48.3 (initial) to 35.0 (3 months) and 22.7 (1 year). At the final follow-up, the EBD group showed 35.1±17.2 (71.2%) improvement in acne severity, whereas the non-EBD group showed 25.6±10.1 (53.0%) improvement compared with their baseline values (Table 3). The mean global improvement score of the EBD group was 3.45±0.61, whereas that of the non-EBD group was 2.50±0.70 (P<0.001). In the RM-ANOVA, a significant effect of the mGAGS with the interaction between time and group allocation was noted (P<0.001) (Figure 2). Post-hoc analysis at each time point revealed that there were significant differences in acne severity at 3 months (P=0.005) and 1 year (P<0.001).

Table 3. Treatment regimens, clinical responses, and side effects

Feature	EBD (n=82)	Non-EBD (n=44)	Total (n=126)	*p* value
Total isotretinoin dose, mg	3378.1±1871.4	4535.0±2350.7	3782.1±2115.9	**0.004**
Drug-related side effects				
Laboratory abnormalities	1/31	2/26	3/57	0.59
Severe dryness	7 (8.5)	12 (27.3)	19 (15.1)	**0.01**
Laser or Energy-based devices				
Needle RF ± AFL	44 (53.7)	NA	NA	NA
PDL ± AFL	24 (29.3)	NA	NA	NA
Needle RF & PDL ± AFL	14 (17.1)	NA	NA	NA
Combined topical therapy*				
Topical retinoid ± BPO	21 (25.6)	11 (25.0)	32 (25.4)	0.99
Topical antimicrobial ± BPO	32 (39.0)	22 (50.0)	54 (42.9)	0.32
Salicylic acid	40 (48.8)	25 (56.8)	66 (51.6)	0.50
Intralesional triamcinolone	39 (47.6)	18 (40.9)	57 (45.2)	0.60
Improvement of mGAGs	35.1±17.2	25.6±10.1	31.8±15.7	**0.004**
Global improvement score	3.45±0.61	2.50±0.70	3.12±0.79	**<0.001**
Relapse after initial efficacy	14 (17.1)	10 (22.7)	24 (19.0)	0.59

*RF, radiofrequency; PDL, pulsed dye laser; AFL, ablative fractional laser; NA, not available; BPO, benzoyl peroxide. Statistically significant P values are in bold. *Patients might be listed in >1 category.*

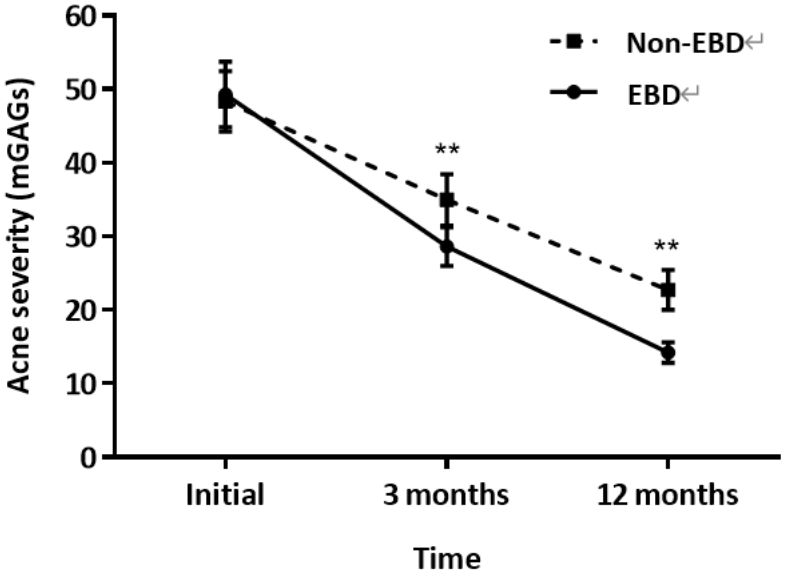

Figure 2. Change in acne severity (modified Global Acne Grading Score) with time and treatment group. ** P<0.017 in post-hoc analysis at each time point.

3. Subgroup analysis

Table 4 shows results of the subgroup analysis of patients in the EBD group. Patients were classified as adult-type acne group (n=24) if the disease occurred or persisted after 25 years of age, if not they were classified as adolescent-type acne group (n=58). If the initial mGAGS of the medial location (chin, nose, and forehead) was higher than that of the lateral side (cheek), we classified patients into a medial group (n=19). Otherwise, we classified patients into a lateral group (n=63). No statistical differences in the mGAGS at each assessment were noted between these groups. Based on type of energy-based interventions, patients were classified into three groups: FMRF ± AFL (n=44), PDL ± AFL (n=24), FMRF combined with PDL ± AFL (n=14). Although there were no significant differences between these three groups, we observed that patients in the FMRF combined with PDL ± AFL group showed the highest improvement rate (73.3%). Additionally, there was no significant difference in the degree of improvement when comparing those who received energy-based intervention treatment more than five times during the study period with those who did not.

4. Clinical factors associated with good treatment response

In the multivariate analysis, initial mGAGS, all energy-based intervention treatment modalities (FMRF ± AFL, PDL ± AFL, FMRF combined with PDL ± AFL), and topical retinoid were independently associated with the improvement of acne (Table 5). Acne severity improved by 25.2% with FMRF combined with PDL ± AFL treatment, followed by 18.1% with FMRF ± AFL treatment and 16.4% with PDL ± AFL treatment. Additionally, final mGAGS decreased by 0.21% per 1-point increment of the initial mGAGS. Age, disease duration, and accumulated isotretinoin dose were not associated with the treatment response.

Table 4. Subgroup analysis in the energy-based intervention treatment group

	Initial	**3 months**	**1 year**	*p* value
Feature	Mean ± standard deviation (improvement rate, %)			
Onset of acne				
Adult-type (n=24)	44.6±15.2	25.7±7.9 (39.5)	14.2±6.7 (67.2)	0.16
Adolescent-type (n=58)	51.2±21.8	29.8±13.2 (39.4)	14.2±6.3 (70.8)	
Location				
Medial (n=19)	51.6±16.6	31.4±13.9 (38.5)	17.5±6.5 (65.2)	0.89
Lateral (n=63)	48.6±21.2	27.8±11.3 (39.7)	13.2±6.0 (71.2)	
Laser or Energy-based devices				
Needle RF ± AFL (n=44)	48.4±20.0	28.6±11.8 (38.3)	14.6±6.1 (68.2)	0.07
PDL ± AFL (n=24)	56.3±18.1	29.9±10.4 (45.2)	15.6±6.5 (70.7)	
Needle RF & PDL ± AFL (n=14)	40.1±21.4	26.4±15.3 (33.0)	10.6±6.0 (73.3)	
Treatment sessions				
≤5 sessions /1 year (n=40)	51.6±22.0	28.1±12.2 (43.0)	13.9±5.8 (71.1)	0.16
>5 sessions /1 year (n=42)	47.1±18.3	29.1±11.8 (36.1)	14.6±6.9 (68.6)	

RF, radiofrequency; PDL, pulsed dye laser; AFL, ablative fractional laser;

Table 5. Univariate and multivariate linear regression analysis of factors associated with acne severity improvement (%).

	Univariate		Multivariate	
Feature	B(SE)	p value	B(SE)	p value
Female gender	-2.72 (2.69)	0.32	-3.44 (2.34)	0.15
Age at the diagnosis, years	0.10 (0.27)	0.71	0.47 (0.25)	0.07
Disease duration (months)	0.009 (0.033)	0.79	-0.05 (0.03)	0.12
Initial mGAGS	0.17 (0.07)	0.20	0.21 (0.07)	**0.005**
Total isotretinoin dose, per 100mg	-0.67 (0.66)	0.30	0.17 (0.63)	0.80
Laser or Energy-based devices				
Non-EBD	Ref		Ref	
Needle RF ± AFL	6.75 (2.77)	0.016	18.1 (3.06)	**<0.001**
PDL ± AFL	8.53 (3.35)	0.012	16.4 (3.46)	**<0.001**
Needle RF & PDL ± AFL	10.8 (4.12)	0.011	25.2 (4.23)	**<0.001**
Combined topical therapy				
Topical retinoid ± BPO	5.38 (3.07)	0.08	7.07 (3.00)	**0.020**
Topical antimirobial ± BPO	-1.15 (2.73)	0.67	2.28 (2.67)	0.40
Salicylic acid	3.00 (2.69)	0.27	2.68 (2.37)	0.26
Intralesional triamcinolone	2.73 (2.70)	0.32	1.09 (2.52)	0.57

B, regression coefficient; SE, standard error; mGAGS, Modified Global Acne Grading Score; RF, radiofrequency; PDL, pulsed dye laser; AFL, ablative fractional laser; BPO, benzoyl peroxide.

Statistically significant P values are in bold.

5. Side effects and relapse rate

Severe dryness of mouth, skin, or eyes, leading to a reduction of isotretinoin intake, occurred more frequently in the non-EBD group than in the EBD group (27.3% vs. 8.5%, *P*=0.01). Elevated levels of triglyceride, liver enzymes, or cholesterol were noted in one patient in the EBD group and two patients in the non-EBD group (Table 3). After energy-based intervention treatment, most patients reported side effects such as transient erythema and edema, which resolved within hours to a few days after treatment. No patient reported severe adverse events or delayed wound healing after the procedure. Relapse after initial successful treatment occurred in 24 (19.0%) patients; there was no significant difference between frequency of relapse in the EBD and non-EBD groups.

IV. DISCUSSION

In this study, we compared the efficacy and safety of using isotretinoin alone and combined use of low-dose isotretinoin and energy-based interventions for treating inflammatory acne. The improvement of mGAGS was significantly better in the EBD group than in the non-EBD group, showing that combined use of systemic isotretinoin with laser or energy-based interventions is more effective for inflammatory acne treatment than the use of oral isotretinoin alone. Our study also demonstrated the long-term efficacy of this combination treatment over a 1-year follow-up period; patients who received the combination treatment showed better clinical outcome in terms of not only early response but also good long-term results. Moreover, we found that the combination treatment is well tolerated and does not cause any serious adverse side effects.

After adjustment in the regression analysis, acne severity was significantly decreased in the EBD group by 18–25% compared with that in the non-EBD group. This finding implies that FMRF, PDL, and AFL have potential benefits to patients with inflammatory acne. FMRF can decrease sebum production, a major pathogenetic factor of acne, through thermal stimulation.[6, 18] Previous studies have demonstrated a considerable reduction of inflammatory acne lesions and non-inflammatory acne lesions after several sessions of FMRF without any serious adverse outcomes.[6-8] PDL inactivates *Propionibacterium acne* via porphyrins' absorption and destroys sebum glands through its thermal effect.[9, 19] Some patients demonstrated a significant reduction of acne counts and a reduction of sebum production after undergoing PDL treatment.[9, 10] The fractional laser generally plays an important role in treating acne scarring.[20] It has been reported that the fractional laser facilitates skin resurfacing and induces anti-inflammatory effects via the upregulation of heat shock proteins.[21] Although the exact role of the fractional laser in inflammatory acne treatment remains unknown, many studies have reported favorable clinical responses after fractional laser treatment.[11, 12, 20]

Despite the proven efficacy of systemic isotretinoin for treating inflammatory acne, it commonly causes side effects such as dry lips, dry eyes, and muscle pain.[21] Some studies have found more serious adverse outcomes such as dermatological events, ocular adverse events, and psychosomatic events.[22] Moreover, the association between teratogenicity in pregnancy and oral isotretinoin use is well documented.[5, 23] In the present study, total isotretinoin doses prescribed for patients were significantly higher in the non-EBD group than in the EBD group. In consequence, the frequency of isotretinoin-related side effects was also higher in the non-EBD group than in the EBD group. Although patients in the EBD group received a lower dose of systemic isotretinoin, they still demonstrated better clinical outcomes and similar relapse rates after the cessation of treatment compared to the non-EBD

group. These findings suggest that the combined treatment of systemic isotretinoin and energy-based interventions could reduce the effective dose of systemic isotretinoin while maintaining good clinical outcomes.

Our results are consistent with those of previously published studies reporting that the combined use of oral isotretinoin with energy-based intervention is well tolerated and does not cause any serious side effects.[13-15, 24] In the current study, transient side effects, such as erythema and edema, were observed in the EBD group. None of the patients had a history of abnormal scarring, delayed wound healing, or other serious adverse outcomes. Moreover, six patients diagnosed with inflammatory acne combined with acne keloidalis showed improvement of 68% in the Vancouver Scar Scale score[25] after receiving 12 months of the combination treatment. Therefore, we can conclude that energy-based interventions, including FMRF, PDL, and AFL, are well tolerated as combination treatment with systemic isotretinoin.

Our subgroup analysis revealed that the improvement rate was relatively higher in patients who underwent FMRF combined with PDL than in those who underwent FMRF or PDL alone, although statistical significance was not achieved. This result suggests that combination treatment using FMRF with PDL has a synergistic effect on patients with inflammatory acne and could be considered as an effective modality for treating inflammatory acne.

The present study had some limitations. First, since our study was performed in a single, tertiary referral center, our cohort does not represent all patients with inflammatory acne in the general population. Second, selection bias may have led to the inclusion of more patients with chronic or recalcitrant acne. Third, the study was limited by its retrospective nature. Fourth, missing or incomplete data could have interfered with the accuracy of the assessment of acne severity, clinical response, and disease recurrence. Lastly, there were statistical limitations due to the small number of patients in each subgroup of

treatment modalities. Nevertheless, in the present study, the effectiveness of a combination treatment for inflammatory acne could be analyzed under relatively uniform conditions in real-world conditions. Moreover, during the 1-year follow-up period, we not only evaluated transient effects of treatment but also demonstrated the long-term effectiveness and adverse outcomes of this treatment in a clinical setting.

Conclusions

In conclusion, combined treatment using low-dose isotretinoin and energy-based interventions shows positive responses and is well tolerated in patients with inflammatory acne. A low dose of systemic isotretinoin was sufficient to maintain good clinical outcomes when used with a combination of energy-based interventions. Thus, combined use of different energy-based interventions could be another promising treatment choice for patients who are aware of systemic isotretinoin-related side effects. Moreover, as the combination treatment also improved acne keloidalis, early treatment of this modality is suggested to be beneficial to patients with inflammatory acne combined with acne keloidalis or patients with inflammatory acne who tend to develop acne scarring. Further investigations regarding combination treatment are warranted to optimize the treatment efficacy of low-dose isotretinoin combined with other energy-based interventions.

List of Abbreviations

EBD, energy-based intervention; FMRF, fractional microneedle radiofrequency; PDL, pulsed dye laser; AFL, ablative fractional carbon dioxide laser; mGAGS, modified Global Acne Grading Score; RM-ANOVA, repeated measures analysis of variance; vs., versus.

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ABSTRACT(IN KOREAN)

염증성 여드름 환자에서 저용량 경구 isotretinoin 제제와 레이저 병용 요법의 효과 및 안정성

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연구배경: 염증성 여드름 환자에서 저용량의 경구 isotretinoin 제제를 투여하면서 fractional microneedle radiofrequency, pulsed dye laser, ablative fractional laser 등의 레이저 치료를 병용하는 것이 질환의 호전에 도움이 될 수 있으나, 현재 이에 대한 효과 및 안전성에 대해서 연구된 바는 없다.

목적: 염증성 여드름 환자를 대상으로 저용량 경구 isotretinoin 제제와 레이저 병용 요법의 효과와 안전성을 살펴보고자 하였다.

방법: 세브란스병원 피부과에 내원한 염증성 여드름 환자의 의무기록을 통해서 후향적 연구를 진행하였으며, 총 126명 중에서 레이저 시행군 82명, 미시행군 44명이 등록되었다.

결과: 1년의 치료 후 레이저 시행군과 미시행군의 Modified global acne grading score는 각각 35.1±17.2, 25.6±10.1점이 호전되었으며, 레이저 시행군에서 통계적으로 유의하게 호전 정도가 더 높았다. 또한 레이저 시행군은 미시행군에 비해 누적

약제 투약량과 약제 관련 부작용 빈도가 통계적으로 유의하게 낮았다.

결론: 염증성 여드름 환자에서 경구 isotretinoin 제제와 레이저 병용 요법은 효과적이면서 안전성이 높은 치료 방법이다.

핵심되는 말: 염증성 여드름; oral isotretinoin; fractional microneedle radiofrequency; pulsed dye laser; ablative fractional laser