Tranilast and Minocycline Combination for Intractable Severe Acne and Prevention of Postacne Scarring: A Case Series

To the Editor:

Patients with severe acne[1] are greatly afflicted by cosmetic problems due to postacne scarring[1,2] that can impair their quality of life. Severe acne[1] is characterized by cysts, nodules, or nodulocystic lesions in which postacne scarring[1,2] occurs frequently.[3] The basic treatment regimen[1] is face washing, external antibiotic agent, and oral antibiotics. Recently, the topical retinoid, adapalene,[4] has been reported to be useful in reducing scar formation in severe acne. Furthermore, this medication[4] has a good safety profile in the treatment of moderate to severe inflammatory acne; however, topical adapalene gel[5] and oral azithromycin showed no significant difference in their effect on severe acne. In recent years, however, tranilast[6,7] (N-[3′,4′-dimethoxycinnamoyl]-anthranilic acid), which inhibits degranulation from mast cells and is primarily a therapeutic agent for allergy, can contribute to a number of biological processes, including wound healing. So far, blocking mast cell function[6,8] by tranilast could be used to prevent or minimize scarring. The combined effects of tranilast 8% liposomal gel[9] with oral isotretinoin have been reported to more effectively reduce scar formation. The aim of this study is to evaluate the effects of oral tranilast on preventing postacne scarring in severe acne patients.

Twelve severe acne patients (7 males and 5 females) of grade 3 or 4 (indicated below) without treatment history at the start of this combination therapy were enrolled (Table 1). The mean age of the participants was 25 (range 14–41) years. At the first visit, there were 6 notable cases of grade 3 or 4 acne in 5 older patients and 1 younger patient (indicated with * in Table 1) with slight or mild atrophic scarring that already existed before the treatment. These patients had a history of recurrent relapse. The severity of acne was clinically graded by combining basic clinical grading with severity grade tables given by Adityan et al[2] as follows: grade 4 = almost entire face involved with numerous papules and pustules, and nodules already present; grade 3 = more than half of the face with many papules and pustules, and a few nodules noted; grade 2 = less than half of the face with recognizable papules and pustules; grade 1 = under 20% scattered lesions with a few papules or pustules; and grade

Table 1. Patients and progress of the combination therapy.

No.	Age/sex	Grade Before combination	Period of treatment/evaluation grade 1 month	2 months	3 months	4 months	5 months
1	14/m	4	3	2	2	1	0
2	17/f	3	2	1	0	NA	NA
3	17/m	3	2	1	0	NA	NA
4	18/m	4*	3	2	2	1	0*
5	20/f	3	2	1	0	NA	NA
6	21/f	3	2	1	0	NA	NA
7	24/m	3	2	1	1	0	NA
8	25/m	4*	3	2	1	1	0*
9	27/m	4*	3	2	1	1	0*
10	39/m	3*	2	1	1	0*	NA
11	39/f	4*	3	2	1	1	0*
12	41/f	4*	3	2	1	1	0*

NA, not attended.
*Notably slight or mild residual scars already presented before the treatment.

0 = clear skin with no inflammatory and scarring lesions. The patients were administered 100 mg/d minocycline and 200 mg/d tranilast for up to 4–5 months depending on each patient's severity. Face washing with soap and clindamycin cream, as routine therapy for acne vulgaris, were performed nightly. Clinical features were evaluated once per month.

Table 1 describes the course of combination therapy. All participants healed almost all their acne lesions without newly developed hypertrophic scars. Severe acne patients (grade 4) took over 5 months to reach grade 0, but patients with grade 3 acne showed recovery after approximately 3–4 months of the combination therapy. Notably, older patients have recurrent severe acne from early age and had not been administered tranilast for severe inflammatory acne. Thereafter, patients with milder lesions of grade 3 preferred better therapeutic effects. However, in most severe cases (grade 4), the treatment should be extended to achieve healing over 4–5 months.

Several chemical mediators from mast cells[6,8] in inflammatory lesions, such as severe acne lesions, may result in the development of scar/keroid. So far, it is expected that tranilast reduces scar formation by suppressing activation of mast cells.[6,8] Moreover, tranilast inhibits the release of transforming growth factor (TGF)-β1 from keloid fibroblasts,[6,7] which enhances the collagen synthesis of keloid fibroblasts in hypertrophic scar tissue, but not healthy skin fibroblasts. The author has previously reported the therapeutic effects of tranilast combination therapy in addition to roxithromycin on uncontrollable prurigo nodularis,[10] which is also believed to be related to the inhibition of excessive collagen production from the amplified dermal fibroblasts by tranilast. Although an improved effect of tranilast gel[9] on acne scars has been reported, systemic tranilast administration will further ensure its effect. Based on these and other findings,[6,7,9] patients with severe acne, especially recurrent acne, can expect a satisfactory therapeutic strategy. The addition of tranilast and suppression of excessive reaction of lesional fibroblasts can result in prevention of postacne scar formation. In Japan, this agent has already been approved for the treatment of hypertrophic scars; so far, it is wasteful for it to be retained only in Japan and Korea.

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REFERENCES

1. Rumman N. A review on the advances in the treatment of moderate to severe acne vulgaris. *Gavin J Dermatol Res Ther.* 2016:26–36.
2. Adityan B, Kumari R, Thappa DM. Scoring systems in acne vulgaris. *Indian J Dermatol Veneol Leprol.* 2009;75:323–326.
3. Layton AM, Henderson CA, Cunliffe WJ. A clinical evaluation of acne scarring and its incidence. *Clin Exp Dermatol.* 1994;19:303–308.
4. Gold LS, Weiss J, Rueda MJ, et al. Moderate and severe inflammatory acne vulgaris effectively treated with single-agent therapy by a new fixed-dose combination adapalene 0.3 %/benzoyl peroxide 2.5 % gel: a randomized, double-blind, parallel-group, controlled study. *Am J Clin Dermatol.* 2016;17:293–303.
5. Ghoshal L, Banerjee S, Ghosh SK, et al. Comparative evaluation of effectiveness of adapalene and azithromycin, alone or in combination, in acne vulgaris. *Ind J Dermatol.* 2007;52:179–183.
6. Suzawa H, Kikuchi S, Arai N, et al. The mechanism involved in the inhibitory action of tranilast on collagen biosynthesis of keloid fibroblasts. *Jpn J Pharmacol.* 1992; 60:91–96.
7. Darakhshan S, Pour AB. Tranilast: a review of its therapeutic applications. *Pharmacol Res.* 2015;91:15–28.
8. Komi DEA, Khomtchouk K, Santa Maria PL. A review of the contribution of mast cells in wound healing: involved molecular and cellular mechanisms. *Clin Rev Allergy Immunol.* 2019. doi: 10.1007/s12016-019-08729-w.
9. Weinstein A, Koren A, Sprecher E E, et al. The combined effect of tranilast 8% liposomal gel on the final cosmesis of acne scarring in patients concomitantly treated by isotretinoin: prospective, double-blind, split-face study. *Clin Exp Dermatol.* 2019. doi: 10.1111/ced.14032.
10. Horiuchi Y, Bae SJ, Katayama I. Uncontrollable prurigo nodularis effectively treated by roxithromycin and tranilast. *J Drugs Dermatol.* 2006;5:363–365.