Combined Treatment of Stromal Vascular Fraction and Ablative Fractional CO₂ Laser for Hypertrophic Foot Scar

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The treatment of keloid and hypertrophic scars (HTSs) remains one of the most difficult challenges, with a high recurrence rate regardless of the method of treatment. The latest trend in scar management is a combined approach using multiple modalities that are individualized to the patient and that would provide successful results for keloid and HTSs. There are previous reports that stromal vascular fraction (SVF) is effective for scar remodeling. Based on these reports, we introduced the concept of a combination treatment using SVF injection and fractional ablative CO₂ laser. In this report, we present a 21-year-old woman who was involved in a car accident. A defect on her foot was covered with a skin graft, but the scars became elevated, which turned out to be HTSs. She was treated with a fractional ablative CO₂ laser for five sessions. A month later, SVF injection and fractional ablative CO₂ laser were conducted simultaneously. The result of a year's follow-up showed a flattened scar with resolution of pigment deposition. In conclusion, the combination treatment for HTSs with SVF injection and ablative fractional CO₂ laser is one of the modalities to achieve an excellent outcome for treating HTS.

Key words

Hypertrophic scar; HTS; Stromal vascular fraction; SVF; Ablative fractional; CO₂ laser

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INTRODUCTION

Hypertrophic scars (HTSs) are elevated scar which occur after trauma, surgical or burn wounds. Abnormal fibrous tissue deposition is characteristic finding of the HTSs and keloids. Peacock et al.¹ defined HTSs as overgrown fibrous tissue that confined in the wound while the keloids extend beyond the original wound.

Treatments that now being used include corticosteroid injection, surgical removal, and energy-based therapies including lasers and radiofrequencies. However, no single method has emerged as the gold standard for HTS. In 2002, Mustoe et al.² recommended corticosteroid injection combined with silicone gel sheeting as first-line therapy and laser treatment and surgery with adjunctive silicone gel sheeting as second-line therapy. In 2014, Gold et al.³ updated recommendations for scar management and concluded that combination approach using multiple modalities that are individualized to patient would provide successful treatment results for HTSs and keloids.

Laser treatment for keloids was first introduced in the 1980s⁴ and its therapeutic use with diverse wavelengths has been investigated. In 2007, Hantash and Mahmood⁵ first introduced the use of fractional ablative CO₂ laser as a resurfacing device. It was suggested that treatment with fractional CO₂ laser is an efficient and safe for therapeutic use in HTSs and keloids.⁶

The stromal vascular fraction (SVF) derived from adipose tissue contains heterogeneous cell populations and

especially adipose-derived stem cells (ASCs) are part of it. SVF injection into HTSs decreased the dermal thickness of the scar.⁷

As a HTSs treatment modality, fractional ablative CO₂ laser and SVF injection proved useful. In this report, we present our experience with novel combined treatment strategy for HTSs with SVF injection and fractional laser treatment.

CASE REPORT

A 21-year-old woman came to visit our clinic for treatment of HTSs. The patient was involved in a car accident six months ago and was injured in left foot. The lacerations were sutured on the day of the accident and the split-thickness skin graft was performed 2 months later on the defect site on the other clinic. The scars were photographed on the first visit to and HTSs were observed in the sutured sites and skin graft margins, accompanied by hyperpigmentation (Fig. 1).

We used a fractional ablative CO₂ laser (LineXel; UTI Co. Ltd., Seoul, Korea) system. The laser procedure was performed with a pulse duration of 140 to 1000 ms and a distance between spots were set at 0.9 mm. Pulse duration was adjusted according to the thickness of scar because the greater the pulse duration, the deeper the penetration depth. Lidocaine and prilocaine mixed cream was applied on treatment site before initiation as a topical anesthetic agent. Fractional ablative CO₂ laser treatment were per-

Fig. 1. Appearance of the patient's foot at the first visit. (A) Dorsal aspect of the left foot, linear hypertrophic scars (HTSs) are seen which assumed to be suture site of the laceration. (B) Medial aspect of the left foot, hyperpigmentation was seen on skin graft and its margin showed HTSs.

Fig. 2. Appearance of the patient's foot after 5 sessions of fractional ablative CO₂ treatment. (A) Dorsal aspect of the left foot, height of the hypertrophic scars (HTSs) seems decreased compared with the Fig. 1. (B) Medial aspect of the left foot, still the color of the HTSs seem reddish purple.

formed every 4 to 6 weeks.

After five sessions of treatment, surgical removal was planned for part of HTSs and SVF injection was performed with the surgery. After a month, under general anesthesia, surgical removal of remaining elevated scar on left foot was carried out. About 4 cm linear zig-zag shaped scar on dorsum of foot, 6 cm linear scar on medial aspect of foot and 3 cm Y shaped linear scar on posterior aspect of foot were excised. After that, Liposuction was performed for SVF extraction. Total amount of 100 ml fat was acquired and sent to laboratory for SVF extraction. Fat tissue was digested in phosphate-buffered saline containing 1% bovine serum albumin and 0.025% collagenase for 80 minutes at 37°C. After processing and purification involving centrifugation and repetitive wash steps, the SVF was suspended in Dulbecco's modified Eagle's medium, and packaged in single-use vial containing $1-1.5 \times 10^6$ cells/ml (Queencell; Anterogen Co., Ltd., Seoul, Korea). 2 vials of SVF was obtained through the process, intradermal injection was performed a day after the surgery. SVF was injected on the whole surface of the HTSs using a 28 gauge needle. Fractional ablative CO₂ laser was carried out immediately after injecting SVF. One year after the injection, the patient's HTSs were diminished and accompanying hyperpigmentation improved (Fig. 3). The patient did not have any noticeable complications.

DISCUSSION

HTSs can cause functional discomfort and cosmetic problems. Still, there is no gold standard for treatment, HTSs remain difficult to manage. HTSs mainly contain type III collagen with nodules containing myofibroblasts and large extracellular collagen filaments.⁸ Transforming growth factor-beta 1 (TGF- β 1) takes critical role in collagen stimulation and also inhibits matrix metalloproteinase expression which result in the accumulation of collagen fibers within the wound.⁹

Mesenchymal stem cells (MSCs) have an anti-scarring effect by means of favoring wound healing during the

process. In 2001, Zuk et al.¹⁰ discovered that ASCs contain multipotent cells and can be used as alternative stem cell source to bone marrow-derived MSCs. Yun et al.¹¹ demonstrated that ASCs reduce activity of myofibroblasts and mast cells resulting in reduced TGF- β 1. After the first injection of ASCs, and antagonistic effects of TGF- β 3 on TGF- β 1 were shown to be high.

Clinical use of ASC for scars was performed in animals, with a pig model and a rabbit ear model. Zhang et al.¹² made a wound on the rabbit ear model and compared the ASCs injection group and the control group after total re-epithelization. The results showed that the scar elevation index improved significantly in the ASCs injection group. Yun et al.¹¹ made a full thickness wound in pig model and compared the ASCs injection group with the control group. The scar size was significantly smaller in the ASC injection group, and the color was similar to the surrounding tissue and the skin stability was better.

Fractional ablative CO₂ lasers can ablate up to 50% of target area and unaffected area remain intact. After laser treatment wound healing process began with migration of epithelial cells from adjacent viable tissue. Because MSCs may accelerate the cutaneous wound-healing process,¹³ SVF injection after laser treatment session may help recovery time short.

Hong et al.¹⁴ demonstrated that early fractional ablative CO₂ laser treatment is effective in minimizing scar formation. In this case, fractional ablative CO₂ laser treatment intervals are equally spaced four to six weeks apart to allow laser treatment to be re-treated in the early remodeling phase. In early remodeling phase, synthesis and degradation are dynamic in the extracellular matrix. Since SVF injection and laser treatment were performed on the early remodeling phase at the same time, it is thought that they would had synergistic effect.

In 2014, international advisory panel on scar management updated consensus guidelines and recommended combination of the therapeutic modalities.³ In this report, we present a novel combination treatment for the HTSs with SVF injection and fractional ablative CO₂ laser. In ad-

Fig. 3. Appearance of the patient's foot 1-year after operation. (A) Dorsal aspect of the left foot, hypertrophic scars (HTSs) were diminished and skin color seems similar with the surrounding tissue. (B) Medial aspect of the left foot, flatten HTSs with improved hyperpigmentation.

dition to that we can expect synergy through a combination of the two modalities.

In this case, some part of HTSs which still were noticeable after five sessions of fractional ablative CO₂ laser treatment were surgically excised and this would result in limitation in identifying the maximum effect of SVF injection. There is no doubt that the effects of SVF injection can be seen elsewhere, since surgical intervention has only been partially involved. In future studies, histologic finding and quantified evaluation will be required. Also, generalized research should be carried out to study the safety and efficacy of this combination therapy.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1. Peacock EE Jr, Madden JW, Trier WC. Biologic basis for the treatment of keloids and hypertrophic scars. *South Med J* 1970;63:755-60.
2. Mustoe TA, Cooter RD, Gold MH, Hobbs FD, Ramelet AA, Shakespeare PG, et al. International clinical recommendations on scar management. *Plast Reconstr Surg* 2002;110:560-71.
3. Gold MH, McGuire M, Mustoe TA, Pusic A, Sachdev M, Waibel J, et al. Updated international clinical recommendations on scar management: part 2--algorithms for scar prevention and treatment. *Dermatol Surg* 2014;40:825-31.
4. Apfelberg DB, Maser MR, Lash H, White D, Weston J. Preliminary results of argon and carbon dioxide laser treatment of keloid scars. *Lasers Surg Med* 1984;4:283-90.
5. Hantash BM, Mahmood MB. Fractional photothermolysis: a novel aesthetic laser surgery modality. *Dermatol Surg* 2007;33:525-34.
6. Azzam OA, Bassiouny DA, El-Hawary MS, El Maadawi ZM, Sobhi RM, El-Mesidy MS. Treatment of hypertrophic scars and keloids by fractional carbon dioxide laser: a clinical, histological, and immunohistochemical study. *Lasers Med Sci* 2016;31:9-18.
7. Wang J, Liao Y, Xia J, Wang Z, Mo X, Feng J, et al. Mechanical micronization of lipoaspirates for the treatment of hypertrophic scars. *Stem Cell Res Ther* 2019;10:42.
8. Slemp AE, Kirschner RE. Keloids and scars: a review of keloids and scars, their pathogenesis, risk factors, and management. *Curr Opin Pediatr* 2006;18:396-402.
9. Spiekman M, Przybyt E, Plantinga JA, Gibbs S, van der Lei B, Harmsen MC. Adipose tissue-derived stromal cells inhibit TGF- β 1-induced differentiation of human dermal fibroblasts and keloid scar-derived fibroblasts in a paracrine fashion. *Plast Reconstr Surg* 2014;134:699-712.
10. Zuk PA, Zhu M, Mizuno H, Huang J, Futrell JW, Katz AJ, et al. Multilineage cells from human adipose tissue: implications for cell-based therapies. *Tissue Eng* 2001;7:211-28.
11. Yun IS, Jeon YR, Lee WJ, Lee JW, Rah DK, Tark KC, et al. Effect of human adipose derived stem cells on scar formation and remodeling in a pig model: a pilot study. *Dermatol Surg* 2012;38:1678-88.
12. Zhang Q, Liu LN, Yong Q, Deng JC, Cao WG. Intralesional injection of adipose-derived stem cells reduces hypertrophic scarring in a rabbit ear model. *Stem Cell Res Ther* 2015;6:145.
13. Sasaki M, Abe R, Fujita Y, Ando S, Inokuma D, Shimizu H. Mesenchymal stem cells are recruited into wounded skin and contribute to wound repair by transdifferentiation into multiple skin cell type. *J Immunol* 2008;180:2581-7.
14. Hong SC, Park ES, Kim YB, Nam SM. Effects of minimizing scar formation by early fractional CO₂ laser resurfacing. *Arch Aesthetic Plast Surg* 2014;20:109-13.