Effect of Topical Vitamin C on Postoperative Carbon Dioxide Laser Resurfacing Erythema

TINA S. ALSTER, MD
TINA B. WEST, MD

BACKGROUND. *Postoperative erythema of several months duration is a universal and problematic side effect of cutaneous carbon dioxide (CO_2) laser resurfacing.*

OBJECTIVE. *This study was conducted in order to determine the effectiveness of two formulations of topical ascorbic acid in reducing the degree and duration of post–CO_2 laser resurfacing erythema.*

RESULTS. *The application of topical L-ascorbic acid in an aqueous formulation resulted in a significant decrease in post–CO_2 laser resurfacing erythema by the eighth postoperative week when compared with laser-irradiated skin that had not received topical vitamin C. The application of topical ascorbic acid in a cream formulation did not result in a significant reduction in post–CO_2 laser resurfacing erythema.*

CONCLUSION. *Topical L-ascorbic acid, when used in an appropriate vehicle and when initiated at an appropriate postoperative period, may decrease the degree and duration of erythema after cutaneous CO_2 laser resurfacing. It is presumed that the anti-inflammatory effect of vitamin C is responsible for the clinical changes observed in this study.* *Dermatol Surg 1998;24:331–334.*

Postoperative erythema of several months duration is a universal and problematic side effect of cutaneous carbon dioxide (CO_2) laser resurfacing. Post–laser resurfacing erythema is related to several factors, including laser-induced tissue thermal injury as well as dermal inflammation, which is associated with the initial stages of the wound healing process with angiogenesis and collagenesis.

Inflammation of the skin, including that induced by inflammatory dermatoses, phototrauma, and CO_2 laser resurfacing, is mediated by free radicals such as reactive oxygen species. Free radicals are molecules or atoms, such as oxygen, with unpaired electrons that attack lipid-rich membranes in the skin, resulting in cell damage. Vitamin C, an antioxidant found normally in human skin, is depleted rapidly in inflammatory states. When L-ascorbic acid (vitamin C) is formulated at a specific concentration and pH level, its penetration through the epidermis is enhanced, effectively delivering 20–40 times the concentration of vitamin C found in normal skin.[1] Based on the known antioxidant effects of ascorbic acid and its ability to be absorbed transcutaneously, this study was conducted to determine whether the use of a topical vitamin C preparation following CO_2 laser resurfacing could reduce the degree and/or duration of post–laser treatment erythema.

From the Washington Institute of Dermatologic Laser Surgery, Washington, DC.

Address correspondence and reprint requests to: Tina S. Alster, MD, 2311 M Street, NW, Suite 200, Washington, DC 20037.

Materials and Methods

Twenty-one patients (one male, 20 females) who had undergone full-face CO_2 laser resurfacing were enrolled in the clinical study after informed consent had been obtained. All patients were at least 18 years of age (age range, 27–67 years; mean age, 44 years). The study was limited to patients with skin types I, II, and III. The same high-energy, pulsed CO_2 laser (UltraPulse; Coherent Laser Corporation, Palo Alto, CA) was used by one operator (TSA) to resurface the skin in all study subjects. Each subject received two to three laser passes using an 8-mm^2 scan with a computer pattern generator (CPG) pattern density of 6, 300 mJ energy density, and 60 W power. Postoperative wound care included continuous topical application of ice and Catrix-10 ointment (Donell Dermedex, Las Vegas, NV). At postoperative day 5–7, all patients were started on a bland petrolatum-based emollient cream (Hydrotone; ICN Pharmaceuticals, Costa Mesa, CA).

Thirteen to 42 days postoperatively (mean, 23.5 days), one-half of each patient's face was randomly selected to receive topical vitamin C prepared (10% ascorbic acid, 2% zinc sulphate, and 0.5% tyrosine) in either an aqueous (11 patients) or cream-based (10 patients) formulation once daily. (This preparation is no longer available. Similar ascorbic acid formulations are distributed by Skinceuticals, Dallas, TX and Cellex-C, Toronto, Canada.) The percutaneous absorption of the cream has been shown to be equal to that of the serum formulation (Dr. Sheldon Pinnell, personal communication). The other half of the face continued to be treated with a bland petrolatum-based emollient cream (Hydrotone). Clinical photographs were obtained at baseline (postoperative day 13–42) and at 2, 4, and 8 weeks after initiating treatment. Cutaneous erythema measurements were recorded with a hand-held reflectance spectrometer (Dermaspectrometer; Cortex Technology, Hagland, Denmark) at study initiation and at each follow-up visit. The spectrometer yields a numerical erythema

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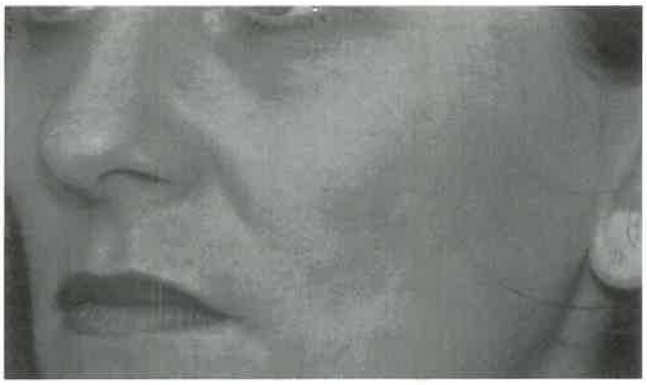

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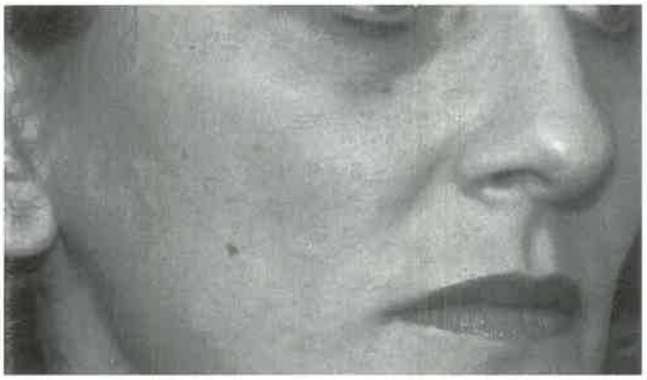

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Figure 1. *A) Untreated (control) facial skin 11 weeks after CO_2 laser resurfacing shows residual patchy erythema. B) Decreased postoperative erythema in L-ascorbic acid-treated facial half in same patient 11 weeks after CO_2 laser resurfacing.*

score by delivering light energy to the skin target, which is then reflected onto a calibrated recording device. Higher numerical values indicate greater erythema. Baseline erythema measurements of untreated skin were taken from the forehead, cheek, and chin area in a random manner bilaterally. The average of these three readings was obtained from each facial half at each follow-up postoperative visit to tabulate results. Statistics were calculated using a standard analysis of variance model.

Results

Twenty patients completed the study. One patient who applied the ascorbic acid serum formulation beginning on the 21st postoperative day developed skin irritation and discontinued the study. Irritation was experienced by a second patient 1 week after beginning serum application (postoperative day 18), but was switched to the cream formulation, which was tolerated without further difficulty. None of the patients experienced irritation or other adverse effects secondary to the use of the cream formulation.

Eight of 10 patients treated with the cream formulation experienced greater improvement in the facial half treated with the ascorbic acid versus the control facial half (Figure 1). The average difference in erythema readings at baseline compared with those obtained at week 8 was 3.86 for the facial half treated with vitamin C cream and 2.53 for the control facial half (Table 1). In one patient, the side treated with emollient showed greater improvement in erythema than the vitamin C–treated side. In one patient, the degree of erythema was equivalent in both facial halves within the 8-week study period. None of the patients treated with the cream preparation experienced irritation. Statistical analysis revealed no significant difference in erythema at week 8 in control versus vitamin C cream–treated facial halves ($P = 0.9626$) (Figure 2).

Eight of 10 patients treated with topical vitamin C serum displayed greater reduction in erythema of the vitamin C–treated facial half compared with the control half. The average difference in erythema readings at baseline versus week 8 was 3.06 for the facial half treated with vitamin C serum and 2.56 for the control nontreated facial half. In one patient, both facial halves showed the same degree of erythema resolution. In two patients, the facial half treated with bland emollient demonstrated greater reduction in erythema than the vitamin C–treated half. Statistical analysis revealed a marginally significant difference in erythema of control

Table 1. Topical Vitamin C Cream: Erythema Readings

		Dermatospectrometer Measurements				
Study No.	*Days of Post-Op*	*Normal Skin*	*Vitamin C Baseline*	*Vitamin C Week 8*	*Control Baseline*	*Control Week 8*
1	33	17	24.0	19.3	23.3	19.7
2	32	14	18.3	14.0	15.7	16.7
3	32	16	19.3	18.0	18.7	18.0
4	13	15	21.0	15.3	21.3	15.3
5	15	14	17.3	17.7	21.0	16.0
6	17	15	19.0	16.0	18.3	16.0
7	19	16	24.0	17.7	22.7	18.0
8	25	17	21.3	20.0	20.0	22.7
9	11	15	27.7	20.7	29.0	22.0
10	18	14	16.3	14.3	15.7	14.3
Mean	21.5	15.3	20.8	17.3	20.6	17.9

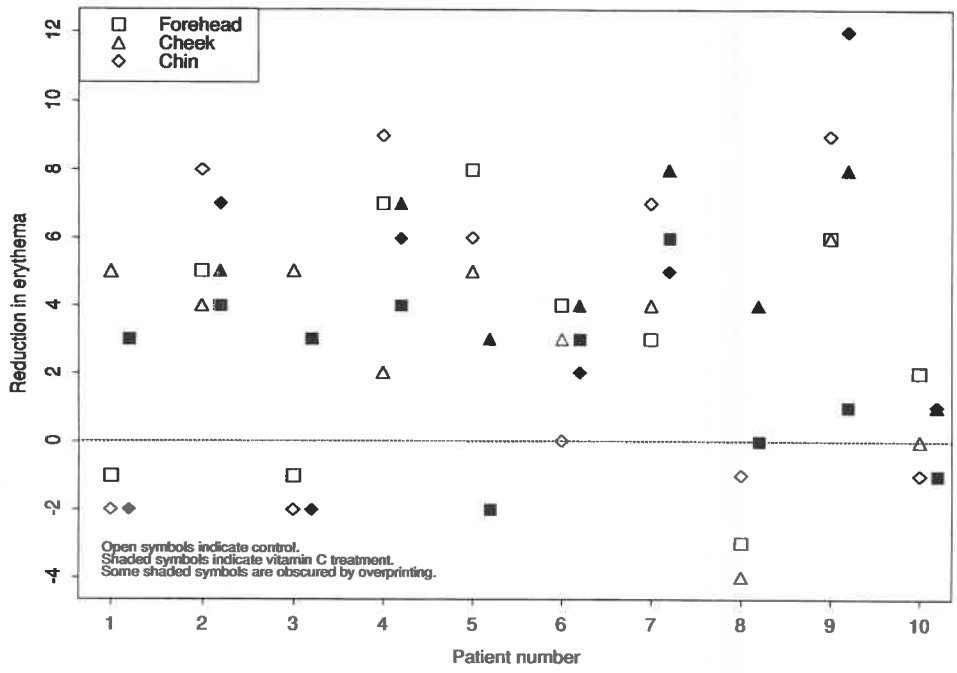


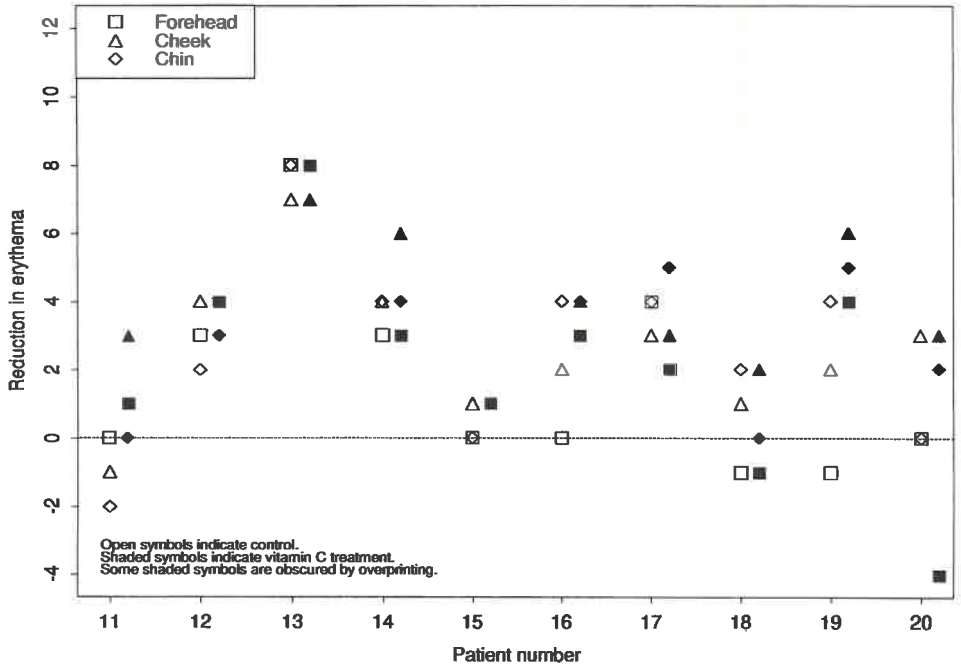
Figure 2. Changes in erythema 8 weeks after administration of vitamin C cream.

versus vitamin C serum–treated facial halves at week 8 ($P = 0.0304$) (Figure 3).

Discussion

Free radicals in the skin are produced as by-products of mitochondrial electron transport. Endogenous dietary antioxidants such as ascorbic acid (vitamin C), tocopherol (vitamin E), and beta carotene limit the levels of prooxidants and their resultant damage to the skin. Enzyme defenses, such as glutathione peroxidase, superoxide dismutase, coenzyme Q-10, and catalase, also prevent oxidant-induced damage to cells.[2] Antioxidants act as potent antiinflammatories. In order for an anti-

Figure 3. *Changes in erythema 8 weeks after administration of vitamin C serum.*



oxidant to be effective in the cell, it must meet three criteria. First, it must be able to reach the target site. Second, it must have greater affinity for free radicals than for the cellular components it is protecting. Finally, the antioxidant must be nontoxic.[3]

Ascorbic acid has been reported to alleviate ultraviolet radiation–induced erythema on porcine and human skin.[4] It can also prevent ultraviolet light–induced immunosuppression.[1,5] In addition to its antioxidant effects, vitamin C plays an important role in collagen synthesis as a cofactor necessary for the cross-linking of the collagen molecule. That ascorbic acid is essential for collagen synthesis has been repeatedly verified by the connective tissue disturbances that occur in scurvy.[6] It is the only antioxidant that has been proven to significantly increase collagenesis.[7] One way ascorbate may stimulate collagen synthesis is by directly and specifically activating collagen gene regulation, both by increasing transcription rate and by stabilizing procollagen mRNA.[8,9] Human skin cells actively transport ascorbic acid. Target sites for vitamin C exist in both the intracellular and intercellular fluid spaces. Ascorbic acid does not work directly in the cell membrane; however, vitamin E, the major antioxidant in the cell membrane, is regenerated by ascorbic acid.[10]

Our study demonstrates that the application of a stable aqueous formulation of 10% L-ascorbic acid (pH 3.5) results in more rapid resolution of erythema as compared with a bland emollient when topical therapy is initiated 2 or more weeks after the laser resurfacing procedure. In addition, the photoprotectant qualities of topical vitamin C make it a beneficial addition to conventional sunscreens for short- and long-term maintenance following CO_2 laser resurfacing. These findings are in accordance with the known antioxidant and antiinflammatory properties of ascorbic acid. Based on our findings, it is likely that topical vitamin C may play an important role in the prevention and treatment of other cutaneous inflammatory conditions as well.

Conclusion

Aqueous topical L-ascorbic acid (vitamin C), when used in an appropriate vehicle and when initiated at an appropriate postoperative period, may decrease the degree and duration of erythema observed after cutaneous CO_2 laser resurfacing. It is presumed that the antiinflammatory effect of this popular antioxidant is responsible for the clinical changes observed in this study.

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