Eyelid Healing After Carbon Dioxide Laser Skin Resurfacing

Histological Analysis

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Objective: To clarify in vivo healing of eyelid skin after carbon dioxide (CO2) laser resurfacing.

Design: Patients requesting upper eyelid blepharoplasty consented to undergo previous CO2 laser skin resurfacing of the upper eyelid skin segments to be excised at various time intervals. After blepharoplasty, the skin specimens were analyzed histopathologically by 2 masked pathologists.

Patients: Eight patients with Fitzpatrick skin types I and II.

Intervention: Upper eyelid CO2 laser resurfacing 1, 2, 4, or 12 weeks before planned upper eyelid blepharoplasty.

Main Outcome Measures: Epidermis: thickness, polarity, contour, and constituents. Dermis: repair zone thickness, vascular and inflammatory pattern, collagen deposition, and elastic fiber changes.

Results: The epidermis regenerated within 7 to 10 days. By 3 months, the epidermis revealed flattening of the rete peg pattern with restoration of polarity, keratinocytes, and melanocytes. The 3-month dermis demonstrated a fibrotic repair zone (500-700 µm), new elastic fibers, and telangiectatic capillaries.

Conclusions: Eyelids heal similarly to other skin regions treated by CO2 laser resurfacing. This cutaneous healing is analogous to that previously reported with use of chemical peels. Histological changes may explain the skin smoothing and wrinkle reduction seen clinically.

PATIENTS, MATERIALS, AND METHODS

Eight patients (4 women and 4 men) requesting cosmetic upper eyelid blepharoplasty were examined to exclude dry eye, exposure keratopathy, eyelid malposition, brow ptosis, and blepharospasm. All patients denied previous herpes simplex infection, systemic fungal disease, immune compromising diseases, tobacco smoking, facial irradiation, skin disease, hypertrophic scarring or keloid formation, and use of isotretinoin (Accutane; Hoffman-LaRoche, Nutley, NJ). Patient skin types were classified as Fitzpatrick types I or II. Patients were given the option to undergo cosmetic laser resurfacing of the eyelids 1, 2, 4, or 12 weeks before blepharoplasty. The risks and benefits of cosmetic laser resurfacing and blepharoplasty were discussed with each patient, who gave informed consent for each procedure.

Carbon dioxide laser skin resurfacing was conducted in standard fashion. Patients were pretreated with a 2% hydroquinone (metahexamide [Melanex; Neutrogena Inc, Los Angeles, Calif]) cream and a broad-spectrum (UV-A and UV-B) sunblock with a sun protective factor of 15 for 6 weeks before laser treatment. In an office setting, patients received regional nerve block with up to 10 mL of 2% lidocaine hydrochloride with 1:100 000 epinephrine in standard fashion. Patients were pretreated with a 2% hydroquinone (metahexamide [Melanex; Neutrogena Inc, Los Angeles, Calif]) cream and a broad-spectrum (UV-A and UV-B) sunblock with a sun protective factor of 15 for 6 weeks before laser treatment. In an office setting, patients received regional nerve block with up to 10 mL of 2% lidocaine hydrochloride with 1:100 000 epinephrine.

In some areas, damaged elastic fibers seemed to be “pushed down” by the infiltrate.

Four weeks after laser resurfacing, the dermis showed a clear diminution in cellularity of the infiltrate. Fusiform fibroblasts were present but much reduced in number. Also, there was an increase in the collagens matrix, between these cells, and less stromal edema and glycosaminoglycan deposition. Thickness of the repair zone was at least 500 µm. Scattered mononuclear cells were present but much less than before. Occasional ecstatic capillaries were noted. Elastic fibers in the repair zone were diminished, if not absent. Three months after laser resurfacing, the dermis revealed only scattered mononuclear cells and occasional foreign body giant cells. Small capillaries within this infiltrate were prominent. The collagen matrix was edematous and full of glycosaminoglycans. An elastic fiber stain indicated variable focal loss of fibers in the papillary and superficial reticular dermis in addition to topical ophthalmic anesthesia (Ophthaine; Alcon Corp, Dallas, Tex).

After standard surgical preparation and installation of protective eye shields, laser resurfacing of the upper eyelids was begun. A CO2 superpulsed laser (NovaPulse; Luxar Corp) set at 9 W was delivered via a collimated handpiece in a standard periorbital pattern. Two passes were applied to each eyelid. Patients received an oral antibiotic (cephalexin hydrochloride, 250 mg twice daily) and an oral antiviral medication (acyclovir hydrochloride, 400 mg three times per day) beginning the day of laser resurfacing and lasting until full reepithelialization occurred. Patients were seen daily until reepithelialization occurred, and then weekly until their planned blepharoplasty.

One man and 1 woman each underwent standard upper eyelid blepharoplasty 1, 2, 4, or 12 weeks after laser skin resurfacing in an ambulatory operating room. The upper eyelid skin removed at blepharoplasty included skin previously treated with the CO2 laser. Skin segments were removed, placed in 10% buffered formalin, and processed for light microscopy with hematoxylin-eosin, Luna-Ishak, Verhoeff-van Gieson (EVG), and Shikata stains. A dermatopathologist (R.G.P.) and an ophthalmic pathologist (A.H.F.), masked to the time intervals and +++, substantial amount.

(Figure 4). In some areas, damaged elastic fibers seemed to be “pushed down” by the infiltrate.

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| Table 1. Eyelid Healing in the Epidermis After Carbon Dioxide Laser Resurfacing |
|-----------------------------|-------------|-------------|-------------|
| Variable                    | 2           | 4           | 12          |
| Thickness, µm               | 100         | 80          | 80          |
| Acanthosis                  | Severe      | Moderate    | Minimal     |
| Basal keratinocytes         | Flat        | Columnar    | Columnar    |
| Melanocytes                 | Few         | Some        | Full        |
| Polarity                    | Abnormal    | Variable    | Normal      |
| Rete peg pattern            | None        | Slight      | Present and flat |

| Table 2. Eyelid Healing in the Dermis After Carbon Dioxide Laser Resurfacing |
|-----------------------------|-------------|-------------|-------------|
| Variable                    | 2           | 4           | 12          |
| Thickness, µm               | 500-700     | 500-700     | 500-700     |
| Fibroblasts                 | Many        | Some        | Few         |
| Inflammatory cells          | Moderate    | Focal       | Few         |
| Blood vessels               | Small capillary | Small capillary | Telangiectasia |
| Matrix                      | +++ Edema   | ++ Edema    | No edema    |
| New collagen                | +           | ++          | +++         |
| Elastic fibers              | Focal loss  | Widespread loss | New         |

*Symbols are as follows: + indicates slight amount; ++, moderate amount; and +++, substantial amount.
Previous histological studies\textsuperscript{3-9} demonstrated that 50 to 150 µm of skin may be ablated with a single pass of a CO\textsubscript{2} laser. The zone of residual thermal (coagulative) damage can extend a further 20 to 120 µm, depending on the particular laser variables used.\textsuperscript{3-9} Because the various CO\textsubscript{2} lasers currently available differ in their biophysical properties, their documented depth of histological ablation and thermal effects vary. Some studies\textsuperscript{3,5,7} document a
progressively increasing zone of thermal damage with each subsequent laser pass, whereas others do not.8,9 We found that profound epidermal and dermal changes occur in the first month after laser resurfacing (Tables 1 and 2).

During the first month after laser skin resurfacing, the epidermis and dermis were significantly altered by cellular atypia, abnormal polarity and differentiation, tissue edema, elastin disruption, and collagen deposition. Three months after treatment many of these changes resolved, and the new epidermis and dermis became more like their untreated counterparts. The contour of the rete pegs remained flatter and smoother than that of healthy, untreated skin. Also, the dermis was thickened by new collagen and elastic fibers parallel to the epidermal surface. Furthermore, abnormal tangiectatic vessels of unknown significance were noted in the dermis 3 months after laser treatment.

Previous studies10-14 evaluating skin healing after CO2 laser resurfacing in other parts of the face consistently demonstrated similar changes to those described herein. One week after laser resurfacing, the dermis-epidermis junction was not seen because of loss of organization.12,13 Three weeks after laser resurfacing, the epidermis was distinct from the dermis, but there is still active inflammation, edema, and immature cells.12-14 Neither the epidermis nor the dermis are normal in appearance. Invariably, all such studies10,11,14 document an increase in collagen and elastin deposition 3 months after laser resurfacing, with a mean increase of 150% to 190%.11 Eyelid skin response to laser resurfacing is similar to that of other facial skin regions, even though eyelid skin lacks a distinct interface between papillary and reticular dermis and subcutis.

Some histological changes reported by others15-18 and herein may be responsible for the clinical observations made after laser resurfacing. Flattening of the rete pegs can smooth skin.16,17 Thermal shrinkage of collagen can reduce the surface area of skin up to 25%.11,18 The deposition of new collagen, particularly glycosaminoglycans, in the dermis can produce thicker skin.19 This may persist beyond 3 months and thus explain the continued wrinkle improvement observed more than 1 year after laser resurfacing.11 Furthermore, the deposition of new elastic fibers in the papillary dermis may improve the appearance of photoaged and elastic skin. There is also anecdotal evidence20 in 2 patients treated with a different CO2 laser than we used of complete loss of elastic fibers in patchy areas after full-face laser skin resurfacing. The exact mechanism and reason for this is not yet known.

There are reported anatomic and molecular changes after laser skin resurfacing whose significance is not fully appreciated. Recently, a porcine skin model of laser resurfacing demonstrated that CO2 laser debridement can reverse the cytologic atypia seen after exposure to a chemical carcinogen.21 Indeed, results of immunohistochemical analysis revealed the presence of contractile actin filaments within the newly deposited fibroblasts after laser resurfacing. These stromal cells might be able to tighten sagging skin and decrease skin creases.

We can only speculate as to the histological changes responsible for the long-term (ie, >1 year) cosmetic effect of laser skin resurfacing. This might be caused by a massive increase in glycosaminoglycans, dermal remodeling, or changes in the newly deposited elastic fibers. Future evaluation of skin healing more than 1 year after laser skin resurfacing may clarify this issue. In addition, biochemical and molecular evaluation of tissue growth modulators and dermal collagen and elastin subunits may elucidate the mechanism of cosmetic skin changes.22 Knowledge gained from such basic scientific research could provide insights for further improvement in the clinical outcomes of laser skin resurfacing.

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