Molecular effects of photodynamic therapy for photoaging.

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Abstract

OBJECTIVE:
To quantitatively examine the epidermal and dermal cellular and molecular changes that occur after photodynamic therapy of photodamaged human skin.

DESIGN:
Serial in vivo biochemical and immunohistochemical analyses after photodynamic therapy using topical 5-aminolevulinic acid (5-ALA) and pulsed-dye laser treatment.

SETTING:
Academic referral center, Department of Dermatology, University of Michigan, Ann Arbor.

PATIENTS:
A volunteer sample of 25 adults, 54 to 83 years old, with clinically apparent photodamage of the forearm skin.

INTERVENTIONS:
Three-hour application of 5-ALA followed by pulsed-dye laser therapy using non-purpura-inducing settings to focal areas of photodamaged forearms and serial biopsy specimens taken at baseline and various times after treatment.

MAIN OUTCOME MEASURES:
Immunohistochemical analysis was used to assess levels of markers of epidermal proliferation (Ki67), epidermal injury (cytokeratin 16), and photodamage (p53), as well as various markers of dermal collagen production (including prolyl 4-hydroxylase and heat shock protein 47, and type I procollagen). Real-time reverse transcriptase-polymerase chain reaction technology was used to quantify type I and type III collagen. Type I procollagen protein was quantified with enzyme-linked immunosorbent assay.

RESULTS:
Epidermal proliferation was stimulated as demonstrated by increases in Ki67 (more than a 5-fold increase; $P < .05$) and epidermal thickness (more than a 1.4-fold increase; $P < .05$). Epidermal injury was produced with increased cytokeratin 16 levels demonstrated (to nearly 70-fold of baseline levels; $P < .05$). Upregulation of collagen production was demonstrated with increases in procollagen I messenger RNA (2.65-fold; $P < .05$), procollagen III messenger RNA (3.32-fold; $P < .05$), and procollagen I protein (2.42-fold; $P < .05$) levels detected. The baseline epidermal p53 level correlated with cytokeratin 16 levels at acute time points, and the latter were found to correlate with peak collagen production.

CONCLUSIONS:
Photodynamic therapy with the specific treatment regimen employed produces statistically significant quantitative cutaneous molecular changes (eg, production of types I and III collagen) that are associated with improved appearance of the skin. Baseline epidermal p53 immunostaining levels may be predictive of dermal responses to this therapy. Comparison with

historical data using pulsed-dye laser therapy alone suggests that use of the photosensitizer may enhance dermal remodeling. The quantitative in vivo molecular data presented herein are in keeping with an evolving model to potentially predict the efficacy of new techniques for the treatment of photoaging.