Topical polyphenolic antioxidants reduce the adverse effects of intense pulsed light therapy

Bruce M. Freedman *
* Plastic Surgery Associates of Northern Virginia, McLean, Virginia, USA

First Published on: 27 May 2009
Topical polyphenolic antioxidants reduce the adverse effects of intense pulsed light therapy

BRUCE M. FREEDMAN

Plastic Surgery Associates of Northern Virginia, McLean, Virginia, USA

Abstract

**Background:** Intense pulsed light therapy (IPL) has been associated with erythema and increased lipid peroxidation. Polyphenolic antioxidants have been shown to decrease inflammation and reduce oxidative stress in irradiated skin. **Objective:** To determine whether the topical application of polyphenolic antioxidants to IPL-treated skin reduced the adverse effects of IPL exposure. **Methods:** In a split-face study, 10 volunteers underwent three full-face IPL treatments (16J/cm², 10ms, 560nm filter) spaced 3 weeks apart. A polyphenolic antioxidant solution was pneumatically applied to the left side of the face, beginning immediately before the first IPL treatment then weekly for six treatments. The lipid peroxide concentration, skin antioxidant level and skin moisture content were obtained before and after the study. **Results:** Skin treated with IPL alone contained a significantly higher concentration of lipid peroxides when compared to skin treated with IPL plus polyphenolic antioxidants \((p<0.05)\). Skin treated with IPL alone contained a significantly lower level of polyphenolic antioxidants and had a significantly lower moisture content \((p<0.05)\). **Conclusions:** In this study, the concurrent pneumatic topical application of polyphenolic antioxidants reduced lipid peroxidation and skin dehydration in IPL-treated skin. Polyphenolic antioxidants may confer a protective effect on facial skin and enhance the effects of IPL therapy.

Key Words: Facial rejuvenation, intense pulsed light, topical antioxidants

Introduction

Intense pulsed light therapy (IPL) has become increasingly popular as a non-ablative modality in skin rejuvenation. IPL systems are high-intensity pulsed sources which emit polychromatic light in a broad wavelength spectrum of 515–1200nm, utilizing selective photothermolysis to target dermal chromophores, deliberately heating and destroying them (1). Clinically, IPL has been shown to decrease facial rhytides, correct dyspigmentation, reduce telangiectasias, and improve skin texture irregularities (2,3). Along with its beneficial effects, IPL exposure has also been associated with erythema, inflammation, and blistering. Additionally, there has been recent evidence to show that IPL exposure can generate oxidative stress, resulting in lipid peroxidation (4).

It has been demonstrated that primary antioxidants can be applied topically to substantially increase their levels in the epidermis and dermis (5). Furthermore, the botanically extracted polyphenol antioxidants have been shown to decrease inflammation, prevent erythema, and decrease carcinogenesis (6,7). Biochemically, these compounds have been shown to prevent radiation-induced oxidation of lipids and proteins by scavenging free radicals and decreasing oxidative stress (8). The purpose of this study was to determine whether the synchronous topical application of polyphenolic antioxidants to IPL-treated skin could reduce the adverse effects of IPL exposure.

Methods

**Patients**

Ten female volunteers with skin phototypes 1–3, aged 36–54 years (average 42 ± 5 years), consented to participate in a split-face, prospective study to evaluate the effects of topical antioxidant application on facial skin that had been treated with IPL. The women were healthy and had no evidence of skin malignancy or active facial acne. The study conformed to the guidelines of the 1975 Declaration of Helsinki.

**Protocol**

Each volunteer underwent IPL treatments delivered by a Sciton Profile System with the Broad Based Light module (Sciton Corporation, Palo Alto, CA, USA).
A series of three full-face IPL treatments spaced 3 weeks apart were performed using the following parameters: 560nm filter; 16J/cm² fluence; pulse duration of 10ms. This corresponded to a calculated fluence rate of ~2500W/cm². Immediately prior to the first IPL treatment and then every 7–10 days for a total of six treatments, an antioxidant rich solution (AntiOx™ 6; Edge Systems Corporation, Signal Hill, CA, USA) containing polyphenolic flavonoids and polyphenolic diterpenes (e.g. epigallocatechin, ursolic acid) was pneumatically applied to the left side of the face. The solution contained no humectants or hydrating agents. The HydraFacial Wave System (Edge Systems Corporation) was used to apply the antioxidant solution at a pressure of 180mmHg. After each treatment, patients were advised to avoid direct sun exposure for 24 hours. Skin care products such as antioxidants, tretinoin and glycolic acid agents were avoided 6 weeks prior to and during the treatment period.

**Skin antioxidant levels**

Skin polyphenolic antioxidant levels were obtained from the left cheek prior to treatment (control) and from both cheeks 1 week following the last treatment. The post-treatment levels from the right cheek reflected levels in skin exposed to IPL therapy, while post-treatment levels from the left cheek reflected levels in skin exposed to IPL therapy plus polyphenolic antioxidants. Skin polyphenolic antioxidant levels were measured using a non-invasive optical device (Biophotonic Scanner, Pharmanex, Provo, UT, USA). This technology employed laser energy at 473 nm and 10 mW of power to stimulate molecules containing carbon–carbon double bonds generating an optical fingerprint. The emitted backscattered light was captured by a highly sensitive light detector, which was then processed and calculated using a Raman scattering spectroscopic technique that has been validated in humans in vivo (9). A linear relationship has been established between antioxidant concentration and Raman intensity, indicating that absolute Raman intensity counts are a biomarker for skin antioxidant levels. These polyphenolic compounds were most likely the biomarkers responsible for the increase. This is due to the fact that these polyphenolic compounds and the carotenoids, which were the biomarkers used by Hata et al., have a comparable spectral Raman peak at 1520 cm⁻¹ (10,11).

**Lipid peroxidation**

Punch biopsy specimens measuring 3 mm in diameter were obtained from the left preauricular area prior to treatment (control) and similar punch biopsy specimens were obtained from the left and right preauricular areas 1 week following the last treatment. Specimens were frozen until assayed. Lipid peroxide concentrations from the right preauricular area reflected levels in skin exposed to IPL therapy, while lipid peroxide concentrations from the left preauricular area reflected levels in skin exposed to IPL therapy plus polyphenolic antioxidants. Lipid peroxidation was assessed by determining the concentration of cutaneous lipid peroxides as described by Sorg et al. (4). Briefly, skin samples were homogenized in methanol containing butylated hydroxytoluene. The homogenates were sonicated and centrifuged and the supernatant separated into two 500mL aliquots. One aliquot was incubated with 50mL of 10mM triphenylphosphine in methanol while 50mL of methanol was added to the other aliquot. A 500mL mixture containing 25mM sulfuric acid, 200mM ammonium ferrous sulfate, 100mM xylene orange and 4mM butylated hydroxytoluene in 90% methanol was then added to both aliquots; optical density was read at 585nm 1 hour later. The specific lipid peroxide signal was obtained by subtracting the non-specific signal (triphenylphosphine) from the global signal. The lipid peroxide concentration was determined using cumene peroxide as a standard (0.5–8.0nmol).

**Skin moisture content**

Water content detection was obtained utilizing interdigital capacitance polyimide film sensor technology (12). Skin moisture content was measured by calculating skin capacitivities using a non-invasive skin probe (MoistSense Skin Sensor, Moritex Corporation, Tokyo, Japan). This methodology was based on determining the dielectric constant or relative permittivity of the skin according to the formula:

\[ C = \frac{\varepsilon \times S}{d} \times (F) \]

where \( C \) = Capacitivities, \( \varepsilon \) = Dielectric constant, \( S \) = Size of sensor surface, \( d \) = Distance between electric poles and \( F \) = Applied force on sensor.

Skin moisture content was measured from the left preauricular area prior to treatment (control) and from the left and right preauricular areas 1 week following the last treatment. Skin moisture content from the right preauricular area reflected levels in skin exposed to IPL therapy, while skin moisture content from the left preauricular area reflected levels in skin exposed to IPL therapy plus polyphenolic antioxidants. All measurements were taken under fixed environmental conditions of 23°C and 50% relative humidity.

**Statistical analysis**

Statistical comparisons of skin polyphenolic antioxidant levels, lipid peroxidation and skin...
moisture content between control and treated tissues were performed using a two-sided paired t-test. Statistical significance was set a priori at $p < 0.05$.

**Results**

After the treatment protocol, the lipid peroxide concentration in IPL-treated skin increased to $260 \pm 30 \text{ nmol/g}$ from the pretreatment control value of $60 \pm 10 \text{ nmol/g}$ ($p < 0.05$). The lipid peroxide concentration in IPL skin treated with topical antioxidants increased to $80 \pm 20 \text{ nmol/g}$; this was not statistically different from control values. However, this concentration was statistically less than the lipid peroxide concentration in IPL-treated skin ($p < 0.05$). Raman intensity counts in pretreated skin (control) was $15000 \pm 2000$. After the treatment protocol, Raman intensity counts in IPL-treated skin was $12500 \pm 2000$, which was statistically less than control values ($p < 0.05$). Raman intensity counts in IPL skin treated with topical antioxidants was $20500 \pm 3000$, a value statistically greater than both control levels and levels determined in IPL-treated skin ($p < 0.05$). After the treatment protocol, the moisture content in IPL-treated skin decreased to $38 \pm 5 \text{ IU}$ from a pretreatment control value of $48 \pm 5 \text{ IU}$ ($p < 0.05$). IPL skin treated with topical antioxidants had a measured moisture content of $68 \pm 10 \text{ IU}$, which was significantly greater than the moisture content measured in the pretreatment control and IPL-treated skin ($p < 0.05$). These data are expressed in Table I.

**Discussion**

As the public’s demand for non-ablative skin treatment has increased, the utilization of light-based therapies has flourished. IPL has gained acceptance in medical offices and spas due to its versatility in treating a wide array of dermatologic conditions rapidly, cost-effectively and with minimal recovery (13). Specifically, the correction of photoaging–diminished fine lines and improved skin texture–has been an area of widespread use for IPL therapy. The mechanism of action includes thermal injury to the dermis which initiates a cascade of inflammatory events including fibroblastic proliferation and apparent up-regulation of collagen expression (14). While IPL has generally been considered safe on account of the moderate dose of visible light used, clinical complications have included edema, erythema, superficial burning and transient pain (1,15). As with many treatments, the mechanisms by which IPL influences biologic tissue may have deleterious as well as beneficial effects. Sorg demonstrated that IPL increased the lipid peroxide concentration in vivo, indicating that oxidative stress could be generated by a moderate dose of visible light delivered through a high fluence rate (4). Recent investigations have shown that visible light can induce indirect DNA damage through the generation of reactive oxygen species and that living systems may be more sensitive to the fluence rates of the radiative stimuli (16,17). In fact, IPL systems can deliver fluence rates of $2000–5000 \text{ W/cm}^2$. It has also been theorized that radiation-induced antioxidant depletion in the skin can lead to altered cellular metabolism (18). The implication is that IPL may not be without photobiologic consequences.

By reducing the potential adverse effects of IPL (e.g. increased free radicals), the safety profile of this prevalent therapy might be improved. Various strategies have been employed to decrease the damaging effects of radiation on the skin. Of note, the topical antioxidants have been shown to scavenge superoxide anions and other radicals, prevent lipid photo-oxidation, and elevate the antioxidative capacity in the skin (19).

(-)-Epigallocatechin-3-gallate, a polyphenolic antioxidant found in green tea, was effective in preventing visible light-induced DNA damage in cultured fibroblasts and keratinocytes (20). Other in vivo studies have concluded that these polyphenolic extracts are effective chemopreventative agents for many of the adverse effects of ultraviolet radiation on human skin (21). Recently, it has been shown that pneumatic application of topical antioxidants produced increased polyphenolic antioxidant levels (22).

In this study, the pneumatic topical application of a polyphenolic antioxidant solution to IPL-treated skin mitigated the previously noted biochemical changes observed after IPL exposure. Lipid peroxide concentration which increased significantly after IPL treatment did not increase significantly when topical antioxidants were applied during the course of IPL therapy (Figure 1). Similarly, skin moisture content decreased significantly after IPL treatment, corroborating a clinical observation that patients often experience ‘dryness’ following IPL exposure.

<table>
<thead>
<tr>
<th>Table I. Results ($n = 10$).</th>
<th>Control</th>
<th>IPL</th>
<th>IPL + antioxidant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipid peroxide concentration (nmol/g)</td>
<td>$60 \pm 10$</td>
<td>$260 \pm 30^*$</td>
<td>$80 \pm 20^t$</td>
</tr>
<tr>
<td>Skin moisture content (IU)</td>
<td>$48 \pm 5$</td>
<td>$38 \pm 8^t$</td>
<td>$68 \pm 10^t$</td>
</tr>
<tr>
<td>Skin polyphenolic antioxidant level (Raman intensity units)</td>
<td>$15000 \pm 2000$</td>
<td>$12500 \pm 2000^*$</td>
<td>$20500 \pm 3000^t$</td>
</tr>
</tbody>
</table>

$^p < 0.05$ vs. control; $^t p < 0.05$ vs. intense pulsed light.
In this study, the topical application of polyphenolic antioxidants during an IPL treatment regimen increased the skin moisture content. This supports other findings that topically applied antioxidants maintained skin barrier function and lessened transepidermal water loss (23,24). Finally, IPL exposure reduced polyphenolic antioxidant levels in the skin. This antioxidant depletion was reversed when topical polyphenolic antioxidants were pneumatically applied during IPL therapy. It has been demonstrated that antioxidants applied after irradiation may not reach the site of action in relevant amounts during the occurrence of oxidative stress (6). Therefore, applying the antioxidants prior to and during the IPL treatment regimen may be important in preserving resident antioxidant populations, resulting in a sustained antioxidative capacity of the skin.

In summary, polyphenolic antioxidants may confer a protective effect on facial skin exposed to visible light radiation and reduce the adverse effects of IPL therapy. Using this information as a foundation, additional research should be conducted to determine whether topically applied antioxidants can enhance the effects of IPL and other light-based therapies.

Acknowledgements
The author would like to acknowledge Jacqueline D. Higgins for her assistance with manuscript preparation and technical support.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References
13. Ross EV. Laser versus intense pulse light: competing technolo-
14. Alam M, Hsu TS, Dover JS, Wrone DA, Arndt KA. Nonabla-
tive laser and light treatments: Histology and tissue effects–A
19. Sato I, Suzeki T, Kobayashi H, Tsuda S. Antioxidative antig-
20. Morley NT, Clifford L, Salter S, Campbell D, Gould D, Curnow A, et al. The green tea polyphenol (–)-epigallocate-
22. Freedman BM. Hydramembrasbrasion: an innovative modal-