Lo último en estética dermatológica

Jorge Soto de Delás
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Current Clinical Practice Recommendation</th>
<th>Controversies or Uncertainties</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhytids</td>
<td>Mild to moderate rhytids can be managed with both ablative and fractionated lasers with greater effects but longer downtimes with ablative lasers. Ultrasoundography and radiofrequency energy can improve rhytids.</td>
<td>Long-term data are lacking regarding ultrasonography and radiofrequency energy. Dyschromia is prevalent with more aggressive treatments. Surgical therapy for more advanced disease is still the gold standard.</td>
</tr>
<tr>
<td>Melasma</td>
<td>Both IPL and nonablative fractionated lasers are safe and effective for melasma and in combination with bleaching agents and superficial chemical peels.</td>
<td>Melasma has a high propensity for recurrence even with more mild treatments; no therapy completely mitigates this risk.</td>
</tr>
<tr>
<td>Facial scarring</td>
<td>Fractionated lasers are safe and effective in acne scarring. They require more treatments than traditional resurfacing lasers, but have a lower adverse effect profile; however, traditional ablation can be used for severe acne scarring.</td>
<td>Dyschromia can occur more frequently with ablative fractionated lasers than nonablative lasers; however, nonablative lasers may only achieve more modest effects. More favorable results may occur by blending treatments.</td>
</tr>
<tr>
<td>Ethnic skin</td>
<td>Ablative resurfacing lasers are contraindicated in Fitzpatrick type V and VI skin; ablative fractionated lasers are relatively safe and effective, but have a risk of dyschromia. Nonablative fractionated lasers are the safest; however, they may require many treatments to achieve expected results.</td>
<td>No laser completely mitigates the risk of dyschromia in Fitzpatrick type V and VI skin. Ultrasonography and radiofrequency may be beneficial for rhytids; however, more data are needed.</td>
</tr>
</tbody>
</table>

Abbreviation: IPL, intense pulsed light.
Facial Erosive Pustular Dermatosis After Cosmetic Resurfacing

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resurfacing procedure</td>
<td>Full-face, fully ablative CO₂ laser</td>
<td>Full-face Jessner solution plus 35% trichloroacetic acid chemical peel</td>
</tr>
<tr>
<td>Laser settings (if applicable)</td>
<td>Three passes. Forehead, cheek and perioral region, 90 mJ. Malar and temporal area, 60 mJ. Lower eyelids, 50 mJ.</td>
<td>Two passes at 150 J and 30 W. For the lower eyelids, 100 J.</td>
</tr>
<tr>
<td>Other procedures performed at time of resurfacing</td>
<td>Upper and lower blepharoplasty</td>
<td>Upper blepharoplasty</td>
</tr>
</tbody>
</table>

JAMA Dermatol. 2017;153(10):1021-1025
Facial Erosive Pustular Dermatosis After Cosmetic Resurfacing

In our own practice, we have seen similar nonhealing wounds after aggressive cryotherapy or electrodessication and curettage in the treatment of nonmelanoma skin cancers on the face or scalp. In addition, we have seen in consultation chronic, erosive facial EPD several weeks to months after fully ablative laser resurfacing. Notably, pustules are frequently absent on physical examination, although intact pustules are not necessary to render an EPD diagnosis. However, erosions and crust seem to be universally present and are the hallmark of the disease. Overall, EPD has been reported mostly on the scalp and upper face and has not been described previously in the perioral, perineal, or perineal regions.
Reconstitution of full-thickness skin by microcolumn grafting

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²Department of Dermatology, Harvard Medical School, Boston, MA, USA
Significant Skin-Tightening by Closure of Fractional Ablative Laser Holes

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Virus-Induced Cancers of the Skin and Mucosa: Are We Dealing with “Smoking Guns” or “Smoke and Mirrors” in the Operating Theatre?

Peter K. C. Goon · Patrick K. Y. Goon · Eunice K. H. Tan · Robin A. F. Crawford · Nick J. Levol · Holger Sudhoff

Received: March 22, 2017 / Published online: May 8, 2017

Dermatol Ther (Heidelb) (2017) 7:290–294
DOI 10.1007/s13555-017-0182-5

BRIEF REPORT

Cancer risk of incremental exposure to polycyclic aromatic hydrocarbons in electrocautery smoke for mastectomy personnel

Hsin-Tsan Tseng · Shih-Ping Lin · Shi-Han Wang · Ling Yang · Shun-Chih Lee · Tao-Jen Lu · Dai-Fen Chen

Environmental Health

Occupational exposures and determinants of ultraviolet particle concentrations during laser hair removal procedures

Emily J. Efferman · Molly L. Lefebvre · Lael S. Adolph · Yinghe Xu · Andrew H. Lee · Serhat Lee · Gary S. Chang · Gary Adamowicz · James E. Hart

Abstract

Background: Occupational exposures to ultraviolet particles on the face generated during laser hair removal procedures, the most commonly performed light-based cosmetic procedures, have not been thoroughly characterized. Acute and chronic exposures to airborne ultraviolet particles have been associated with an increased risk for respiratory and cardiovascular health effects. This study aimed to measure airborne concentrations of particles in a diameter size range of 10 to 100 μm in procedure rooms during laser hair removal procedures.

Methods: Using TEOM 1400 i Calibration Particle Counter, particle concentrations were measured in six procedure rooms in the operating and procedure rooms of a dermatology office. Particle concentrations were sampled before and during and after laser hair removal procedures and characteristics of each procedure were recorded by performing dermatology.

Results: Particle concentrations were sampled over 1 week. Mean ultraviolet particle concentrations in the operating and procedure rooms were 17.49 and 17.16 particles/cm³, respectively. Compared to background ultraviolet particle concentrations before the procedure. The median concentration in the procedure room was 2.05 particles/cm³ greater during the procedure (p=0.002) and 2.05 particles/cm³ greater after the procedure (p=0.002). Duration of procedures (p=0.002), the use of laser hair removal (p=0.002), and the use of more than one laser of type (p=0.002) were the most important variables of airborne particle concentrations. Use of a smoke evacuator (p=0.002) recommended for laser hair removal, but was not statistically significant predictor (p=0.049).

Conclusions: Laser hair removal procedures can generate high numbers of ultrafine particles for dermatologists and other individuals performing laser hair removal with exposure varying based on multiple determinants.

Keywords: Laser, Ultraviolet particles, Surgical smoke, Laser hair removal, Occupational exposure.
RESEARCH LETTER

Awareness of Surgical Smoke Risks and Assessment of Safety Practices During Electrosurgery Among US Dermatology Residents

JAMA Dermatol. 2017;153(5):467-468
Smoke-evacuating cautery pencils for dermatologic surgery

Brett C. Neill, BA, and Nicholas J. Golda, MD

Columbia, Missouri

Fig 1. Smoke evacuation pencil by manufacturer (depicted alphabetically): A, Buffalo Filter’s PlumePen Pro, © 2017 Buffalo Filter LLC. All Rights Reserved. B, ConMed’s GoldVac Smoke Evacuation Pencil, © CONMED Corporation 2017. C, Ethicon/Megadyne’s Zip-Pen, © Ethicon, Inc. (2017). Reproduced with permission. D, Medtronic/Covidien’s Valleylab Smoke Evacuation Pencil, all rights reserved. Used with the Permission of Medtronic. E, Stryker’s Neptune E-SEP Smoke Evacuation Pencil; Stryker Corporation or its affiliates own, use, or have applied for the following trademarks or service marks: E-SEP, Neptune, SealShut and Stryker. All other trademarks are trademarks of their respective owners or holders. (Pricing is variable based on individual contracts, but the units cost approximately $30 each.)
**BRIEF REPORT**

**Autologous Induced Stem-Cell-Derived Retinal Cells for Macular Degeneration**


**SUMMARY**

We assessed the feasibility of transplanting a sheet of retinal pigment epithelial (RPE) cells differentiated from induced pluripotent stem cells (iPSCs) in a patient with neovascular age-related macular degeneration. The iPSCs were generated from skin fibroblasts obtained from two patients with advanced neovascular age-related macular degeneration and were differentiated into RPE cells. The RPE cells and the iPSCs from which they were derived were subject to extensive testing. A surgery that included the removal of the neovascular membrane and transplantation of the autologous iPSC-derived RPE cell sheet under the retina was performed in one of the patients. At 1 year after surgery, the transplanted sheet remained intact, best corrected visual acuity had not improved or worsened, and cystoid macular edema was present. (Funded by Highway Program for Realization of Regenerative Medicine and others: University Hospital Medical Information Network Clinical Trials Registry [UMIN-CTR] number, UMIN000011929.)

**BRIEF REPORT**

**Vision Loss after Intravitreal Injection of Autologous “Stem Cells” for AMD**

Ajay E. Kuriyan, M.D., Thomas A. Albini, M.D., Justin H. Townsend, M.D., Marianeli Rodriguez, M.D., Ph.D., Hemang K. Pandya, M.D., Robert E. Leonard II, M.D., M. Brandon Parrott, M.D., Ph.D., Philip J. Rosenfeld, M.D., Ph.D., Harry W. Flynn, Jr., M.D., and Jeffrey L. Goldberg, M.D., Ph.D.

**SUMMARY**

Adipose tissue–derived “stem cells” have been increasingly used by “stem-cell clinics” in the United States and elsewhere to treat a variety of disorders. We evaluated three patients in whom severe bilateral visual loss developed after they received intravitreal injections of autologous adipose tissue–derived “stem cells” at one such clinic in the United States. In these three patients, the last documented visual acuity on the Snellen eye chart before the injection ranged from 20/30 to 20/200. The patients' severe visual loss after the injection was associated with ocular hypertension, hemorrhagic retinopathy, vitreous hemorrhage, combined traction and rhegmatogenous retinal detachment, or lens dislocation. After 1 year, the patients’ visual acuity ranged from 20/200 to no light perception.
The Risk of Skin Necrosis Following Hyaluronic Acid Filler Injection in Patients with a History of Cosmetic Rhinoplasty.

Robati RM¹, Moeineddin F², Almasi-Nasrabadi M¹.
Platysma Bands: Is a Change Needed in the Surgical Paradigm?

Patrick Trévison, M.D.
Gisella Czukosiamilla, M.D.

Background: Platysma bands are one of the first signs of aging of the neck. Current theories suggest that these bands develop because of skin sagging followed by loss of muscle tone. Treatment strategies therefore aim to tighten skin and muscle. The aim of the present study was to demonstrate that platysma bands are caused by muscular activity during the aging process and are not secondary to skin sagging. This suggests a new approach to managing platysma bands.

Methods: The authors conducted a descriptive, prospective clinical study of 25 patients who presented with definitive, unilateral, facial palsy following one-stage surgical treatment. The authors targeted their observations on anterior neck bands. Patients were followed for up to 10 years.

Results: Of the 25 patients, 76 percent had visible platysma bands on the healthy side, but not on the paralyzed side, of their face. Platysma bands were present on both sides in the 22 percent of patients who had a spastic form of facial palsy. There was no worsening of the platysma band appearance in any patient. No ptosis of the neck skin on the paralyzed side was observed.

Conclusions: This study demonstrated that platysma bands are not related to relaxation of the platysma and skin laxity, but are caused by activity of the platysma muscle. The skin follows the muscle. These observations support a change in surgical management of the aging neck, moving from tightening the skin to denervating the platysma muscle. Further studies need to fully characterize the efficacy and safety of platysma muscle denervation in this indication. (Plast. Reconstr. Surg. 139: 41, 2017.)

Fig. 4. An 80-year-old woman with right facial palsy and bony left muscular band. Even at this advanced age, there is no ptosis of the skin of the neck on the paralyzed side. (Reprinted with permission from Expert2Expert.)

Fig. 5. Fresh cadaver dissection that shows the cervical branch of the facial nerve going toward the platysma muscle. The distance between the mandibular angle and the cervical branch of the facial nerve is approximately 2 cm. (Reprinted with permission from Expert2Expert.)
The Facial Platysma and Its Underappreciated Role in Lower Face Dynamics and Contour

Ada R.T. de Almeida, MD,* Alessandra Romiti, MD,* and Jean D.A. Carruthers, MD, FRCSC, FRC (OPHTH)†

Dermatol Surg 2017; 43:1042–1049

TABLE 1. Demographic Characteristics of Treated Subjects

<table>
<thead>
<tr>
<th></th>
<th>28–73</th>
<th>56.5</th>
<th>57.5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Median</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>142</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Botulinum toxin A</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OnabotulinumtoxinA</td>
<td>131</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IncobotulinumtoxinA</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AbobotulinumtoxinA</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dose/side</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mentalis (M)/platysma</td>
<td>2U/14U</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 3. Cadaver dissection showing the platysma pars modiolaris which fibers are posterolateral to the depressor angulis oris (left). Its contraction contributes to the appearance of lower vertical deep smile lines located lateral to the oral commissures and lateral to melomental folds (right).
The Facial Platysma and Its Underappreciated Role in Lower Face Dynamics and Contour

Ada R.T. de Almeida, MD,* Alessandra Romiti, MD,* and Jean D.A. Carruthers, MD, FRCS, FRC (OPHTH)

Dermatol Surg 2017; 43:1 042–1049
### TABLE 2. Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>1 Treatment Session</th>
<th>≥ 2 Treatment Sessions</th>
<th>Total</th>
<th>p (Fisher’s Exact Test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n Treatment sessions</td>
<td>58</td>
<td>42</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Headache</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1.000</td>
</tr>
<tr>
<td>Alopecia</td>
<td>3</td>
<td>5</td>
<td>8</td>
<td>.275</td>
</tr>
<tr>
<td>Local edema (days postsession), mean (SD)</td>
<td>8.6 (5.3)*</td>
<td>5.8 (4.8)f</td>
<td>7.7 (5.3)</td>
<td>.00014†</td>
</tr>
<tr>
<td>Local numbness (days postsession), mean (SD)</td>
<td>28.4 (11.6)i</td>
<td>28.6 (11.4)j</td>
<td>28.5 (11.4)</td>
<td>.608†</td>
</tr>
<tr>
<td>Local tenderness (days postsession), mean (SD)</td>
<td>3.1 (3.3)¶</td>
<td>3.7 (3.6)#</td>
<td>3.5 (3.5)</td>
<td>.356‡</td>
</tr>
<tr>
<td>Paresis, n (days postsession for resolution)</td>
<td>2 (17, 22)</td>
<td>0</td>
<td>2</td>
<td>.226‡</td>
</tr>
<tr>
<td>Bruising, n</td>
<td>10</td>
<td>13</td>
<td>23</td>
<td>.538**</td>
</tr>
</tbody>
</table>

*Figure 1. (A) Landmarks/identification of area of submental fat distribution; (B) injection pattern; (C) location of needles in the preplatysmal fat.
Conclusions

Although patients are often averse to surgery, the clinicians are responsible (whether they provide both services) for discussing the risks and benefits of and alternatives to any proposed treatment. Although the US Food and Drug Administration indication for deoxycholic acid is moderate to severe submental fat reduction, we propose that deoxycholic acid is better suited for patients with mild to moderate submental liposis, and cost efficacy should be discussed after an estimation of how many vials will be needed in each session to be performed. If the cost of the drug to the patient decreases and the safety profile is further manifest, deoxycholic acid may become more popular. This study suggests that clinicians consider submental liposuction as a superior alternative in regard to cost and recovery for patients who will require more than 2 vials per treatment and more than 3 treatment sessions.
Population Health Implications of Medical Tourism


Background: Fifteen million U.S. patients each year seek medical care abroad. However, there are no data on outcomes and follow-up of these procedures. This study aims to identify, evaluate, and survey patients presenting with complications from aesthetic procedures performed abroad in order to estimate their cost to the U.S. health care system.

Methods: A single-center retrospective review was conducted. A cohort of patients presenting with complications from aesthetic procedures performed abroad was identified. Demographic, complication, and cost data were compiled. Patients were surveyed to assess their overall experience.

Results: Over a 12-month period, 62 patients met inclusion criteria (one man and 41 women), with an average age of 65 ± 14 years (range, 30 to 84 years). Common complications included four active smokers, nine patients with diabetes, and one patient with a history of previous surgery. Average body mass index was 27 ± 4.4 kg/m² (range, 22 to 35 kg/m²). Procedures performed abroad included abdominoplasty (40, repair of hernia (29, liposuction (19), and breast augmentation (15), with several patients undergoing combined procedures. Eren patients presented with histories and eight presented with severe dermal loss. Eight of the 10 patients who were surveyed were not pleased with their results, and 11 would not go abroad again for subsequent procedures. Average costs of treating the complications were $15,251, with an average cost in the U.S. health care system of $3,551. The main payer group was Medicaid.

Conclusions: Complications from patients seeking aesthetic procedures abroad will continue to increase. Patients should be encouraged to undergo cosmetic surgery in the United States to improve patient outcomes and satisfaction and to reduce the economic burden on the health care system.

Clinical Question: Level of Evidence: Therapeutic, IV.

Medical tourism is a growing phenomenon, with an estimated 15 million patients in the United States seeking medical care abroad every year. This represents a $15 billion opportunity cost for U.S. clinicians. Increasing demand for affordable aesthetic procedures and promises of reduced costs are leading many patients abroad to countries such as the Dominican Republic and Mexico. A survey of 100 U.S. plastic surgeons showed that the majority of them had experience treating patients and the sequelae that resulted for those who had traveled abroad for plastic surgery procedures. Almost all surgeons who participated in the survey felt that medical tourism was a trend that had increased or stayed the same over the past 5 years.1,2 It is our responsibility to critically evaluate the risks-benefit ratio of medical tourism and its effect on both our practice of medicine and our patients. For patients interested in aesthetic surgery, medical tourism allows for potentially lower overall costs, increased privacy, and a relationship-based recuperation.3 For plastic surgeons, the benefits of engaging in medical tourism include collaboration with

Disclosure: The authors have no financial interest to declare in relation to the contents of this article.

A “Hot Topic” Video by Editor-in-Chief Rod J. Rohrich, M.D., accompanies this article. Go to FRSJournal.com and click on “Plastic Surgery Hot Topics” in the “Digital Media” tab. On the iPad, tap on the Hot Topics icon.

www.FRSJournal.com

Are you a Canadian thinking about going abroad for surgery or other medical care?

This is referred to as medical tourism. Here's some important information for you to consider before deciding whether or not to become a medical tourist.

My Health

- Traveling abroad for care might generate unforeseen costs
- Before you decide whether to go, contact your travel insurance agency to see if emergency hospitalization or other incurred events are covered.

My Home

- Some types of medical care require follow-up appointments or aftercare treatments
- Before you decide whether to go, make sure that you will be able to get the aftercare (e.g., blood tests) or follow-up appointments you need by talking to your regular doctor here about this.

My Journey

- Not all countries have the same patient and consumer protection laws we have here in Canada
- Before you decide whether to go, learn about malpractice laws in the countries you are considering visiting and make certain that your rights as a patient will be protected.

- Some countries offer medical procedures to international patients that you cannot get here in Canada
- Before you decide whether to go, find out if the procedure you are considering has been shown to be safe and effective by an agency you find reputable.

- Health care is a scarce resource around the world
- Before you decide whether to go, inform yourself about the most pressing health care challenges in the countries you are thinking about visiting and consider whether medical tourism may help or worsen them.

For more information go to www.sfu.ca/medicaltourism/guide

ORIGINAL ARTICLE

Moisturizers are effective in the treatment of xerosis irrespectively from their particular formulation: results from a prospective, randomized, double-blind controlled trial

J.H. Shim,1,*, J.H. Park,1 J.H. Lee,1,2 D.Y. Lee,1 J.H. Lee,1 J.M. Yang1

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2Department of Medical Device Management & Research, SAIHST, Sungkyunkwan University, Seoul, Korea
*Correspondence: J.H. Lee. E-mail: bel711@hanmail.net

Abstract

Background Many companies claim that their moisturizers are superior to others based on their ingredients.

Objective To compare the efficacy and safety of the most popular moisturizers in the field.

Methods A randomized, double-blind, controlled study was performed on 80 patients with moderate to severe xerosis. The test agents included the newly developed cream containing topical recombinant human epidermal growth factor (EGF), its vehicle without EGF and four additional therapeutic moisturizers. The study subjects applied the test agents on designated skin areas twice daily for 4 weeks. All of the clinical assessments and non-invasive objective measurements were performed at baseline, and on days 14 and 28 of the study.

Results All of the test agents significantly improved the clinical symptoms of xerosis. The biophysical parameters similarly improved from baseline (P < 0.05). None of the test agents performed significantly better than did another.

Conclusion In the treatment of xerosis, consistent and regular moisturizing was much more important than the moisturizer’s particular formulation.

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JEADV 2016, 30, 276–281
Epidermal Dysfunction Leads to an Age-Associated Increase in Levels of Serum Inflammatory Cytokines

Lizhi Hu1,2, Theodora M. Mauro1,2,3, Erle Dang1,2,4,5, George Man1, Jing Zhang1, Dale Lee2, Gang Wang3, Kenneth R. Feingold1,2, Peter M. Elias2 and Miao-Qiang Man2

Even though elderly populations lack visible or other clinical signs of inflammation, their serum cytokine and C-reactive protein levels typically are elevated. However, the origin of age-associated systemic inflammation is unknown. Our previous studies showed that abnormalities in epidermal function provoke cutaneous inflammation, and because intrinsically aged skin displays compromised permeability barrier homeostasis and reduced stratum corneum hydration, we hypothesized here that epidermal dysfunction could contribute to the elevations in serum cytokines in the elderly. Our results show first that acute disruption of the epidermal permeability barrier in young mice leads not only to a rapid increase in cutaneous cytokine mRNA expression but also an increase in serum cytokine levels. Second, cytokine levels in both the skin and serum increase in otherwise normal, aged mice (>12 months). Third, expression of tumor necrosis factor-α and amyloid A mRNA levels increased in the epidermis, but not in the liver, in parallel with a significant elevation in serum levels of cytokines. Fourth, disruption of the permeability barrier induced similar elevations in epidermal and serum cytokine levels in normal and athymic mice, suggesting that T cells play a negligible role in the elevations in cutaneous and serum inflammatory cytokines induced by epidermal dysfunction. Fifth, correction of epidermal function significantly reduced cytokine levels not only in the skin but also in the serum of aged mice. Together, these results indicate that the sustained abnormalities in epidermal function in chronologically aged skin contribute to the elevated serum levels of inflammatory cytokines, potentially predisposing the elderly to the subsequent development or exacerbation of chronic inflammatory disorders.

Anti-aging pharmacology in cutaneous wound healing: effects of metformin, resveratrol, and rapamycin by local application

Pan Zhao,1,2,3 Bing-Dong Su,1,2,3 Na Liu,1,2,4 Ya-Bie Lu,1,5 Chen-Xi Zheng,1,5 Yong-Bu Lu,2 Wen-Tao Huang,2 Cui-Hong Zhou,1, J. Chen,2 Dan-Lin Pang,1,5 Dong-Dong Fei,1 Kun Xuan,1,5 Cheng-Hu He1,5 and Yan Jia1,5
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Summary

Cutaneous wounds are among the most common soft tissue injuries and are particularly hard to heal in aging. Caloric restriction (CR) is well documented to extend longevity pharmacologically, profound rejuvenative effects of CR mimetics have been uncovered, especially metformin (MET), resveratrol (RSV), and rapamycin (RAPA). However, locally applied impacts and functional differences of these agents on wound healing remain to be established. Here, we discovered that chronic topical administration of MET and RSV, but not RAPA, accelerated wound healing with improved epidermis, hair follicles, and collagen deposition in young rodents, and MET exerted more profound effects. Furthermore, locally applied MET and RSV improved vascularization of the wound beds, which were attributed to stimulation of adenosine monophosphate-activated protein kinase (AMPK) pathway, the key mediator of wound healing. Notably, in aged skin, AMPK pathway was inhibited, correlated with impaired vasculature and reduced healing ability. As therapeutic approaches, local treatments of MET and RSV prevented age-related AMPK suppression and angiogenic inhibition in wound beds. Moreover, in aged rats, rejuvenative effects of topically applied MET and RSV on cell viability of wound beds were confirmed, of which MET showed more prominent anti-aging effects. We further verified that only MET promoted wound healing and cutaneous integrity in aged skin. These findings clarified differential effects of CR-based anti-aging pharmacology in wound healing, identified critical angiogenic and rejuvenative mechanisms through AMPK pathway in both young and aged skin, and unraveled chronic local application of MET as the optimal and promising regenerative agent in treating cutaneous wound defects.

Keywords: aged skin; AMPK pathway; anti-aging pharmacology; metformin; vascularization; wound healing.

Introduction

Cutaneous wounds are among the most common soft tissue injuries that require long healing cycle during which severe structural and functional damages or further infection sometimes occur (Shaw & Martin, 2009). Particularly, aging is accompanied by an increasing risk of chronic nonhealing cutaneous wounds, resulting in severe clinical burdens but without effective therapeutics (Sigal & Gruber, 2013). Currently, the only intervention shown conclusively to counteract aging in cutaneous restriction (CR) (Fontana & Partridge, 2015), which was also reported to improve wound healing in mammals (Nied et al., 1996). Pharmacologically, several CR mimetics have recently been discovered to retard aging and alleviate age-related pathological changes in various experimental models (Varraman et al., 2016), particularly metformin (MET) (Tamkale et al., 2016), resveratrol (RSV) (Park et al., 2012), and rapamycin (RAPA) (Wilkinson et al., 2012). Among these anti-aging agents, surprisingly, RAPA has been documented to inhibit wound healing (Mills et al., 2008), probably due to its immunosuppressive capability upon systemic administration (Mills et al., 2008; Lamming et al., 2013). However, the effects of other CR mimetics MET and RSV on cutaneous wound healing are less understood. Furthermore, considering that local application of agents on skin is more convenient and may exclude potential systemic side effects, elucidating and comparing topological effects of these anti-aging pharmacological agents on wound healing are of significance to develop clinical relevant strategies for skin defects.

MET, RSV, and RAPA modulate several main signaling pathways mediating CR effects, such as the adenosine monophosphate-activated protein kinase (AMPK) pathway, the sir2 enhancer (SIR2) pathway, and the mammalian target of rapamycin (mTOR) pathway (Varraman et al., 2016). MET, a hypoglycemic agent and AMPK activator, has long been used to treat diabetic hyperglycemia, which substantially improves wound healing (Madison et al., 2014). However, controversial results exist regarding whether AMPK activation by MET improves healing of diabetic wounds, in that negative effects on foot ulcers (Ochoa-Gonzalez et al., 2016) and positive effects on gastric ulcers (Barros & Daff, 2011) upon oral administration of MET have been both reported, suggesting differential effects of MET by systemic and local applications. RSV, a natural polyphenol in red wine and grapes, stimulates both SIRT1 and IAK4 pathways, leading to activation of the metabolic regulator p53 (Singh & O'Brien, 2009; O'Brien et al., 2012).
Anti-Aging Potentials of Methylene Blue for Human Skin Longevity

Zheng-Mei Xiong, Mike O’Donovan, Linlin Sun, Ji-Young Choi, Margaret Ren & Kan Cao

Oxidative stress is the major cause of skin aging that includes wrinkles, pigmentation, and weakened wound healing ability. Application of antioxidants in skin care is well accepted as an effective approach to delay the skin aging process. Methylene blue (MB), a traditional mitochondrial-targeting antioxidant, showed a potent ROS scavenging efficacy in cultured human skin fibroblasts derived from healthy donors and from patients with progeria, a genetic premature aging disease. In comparison with other widely used general and mitochondrial-targeting antioxidants, we found that MB was more effective in stimulating skin fibroblast proliferation and delaying cellular senescence. The skin irritation test, performed on an in vitro reconstructed 3D human skin model, indicated that MB was safe for long-term use, and did not cause irritation even at high concentrations. Application of MB to this 3D skin model further demonstrated that MB improved skin viability, promoted wound healing and increased skin hydration and dermis thickness. Gene expression analysis showed that MB treatment altered the expression of a subset of extracellular matrix proteins in the skin, including upregulation of elastin and collagen 1A1, two essential components for healthy skin. Altogether, our study suggests that MB has a great potential for skin care.
Skin damage mechanisms related airborne particulate matter exposure
Magnani ND. Toxicol Sci. 2016;149: 227-236
Prenatal Air Pollution and Newborns' Predisposition to Accelerated Biological Aging

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**Importance** Telomere length is a marker of biological aging that may provide a cellular memory of exposures to oxidative stress and inflammation. Telomere length at birth has been related to life expectancy. An association between prenatal air pollution exposure and telomere length at birth could provide new insights in the environmental influence on molecular longevity.

**Objective** To assess the association of prenatal exposure to particulate matter (PM) with newborn telomere length as reflected by cord blood and placental telomere length.

**Results** In 641 newborns, cord blood and placental telomere length were significantly and inversely associated with PM$_{2.5}$ exposure during midgestation (weeks 12-25 for cord blood and weeks 15-27 for placenta). A 5-μg/m$^3$ increment in PM$_{2.5}$ exposure during the entire pregnancy was associated with 8.8% (95% CI, −14.1% to −3.1%) shorter cord blood leukocyte telomeres and 13.2% (95% CI, −19.3% to −6.7%) shorter placental telomere length. These associations were controlled for date of delivery, gestational age, maternal body mass index, maternal age, paternal age, newborn sex, newborn ethnicity, season of delivery, parity, maternal smoking status, maternal educational level, pregnancy complications, and ambient temperature.

**Conclusions and Relevance** Mothers who were exposed to higher levels of PM$_{2.5}$ gave birth to newborns with shorter telomere length. The observed telomere loss in newborns by prenatal air pollution exposure indicates less buffer for postnatal influences of factors decreasing telomere length during life. Therefore, improvements in air quality may promote molecular longevity from birth onward.
Cell Reports
Caloric Restriction Promotes Structural and Metabolic Changes in the Skin

Graphical Abstract

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In Brief
Caloric restriction significantly increases the lifespan, but its effect on the skin is poorly understood. Forni et al. show that caloric restriction changes the structure and metabolism of the skin; these changes affect whole-body thermoregulation.

Highlights
- Caloric restriction (CR) remodels the skin and fur and expands the local stem cell pool
- CR promotes metabolic reprogramming in both the dermis and epidermis
- CR imposes a thermoregulatory challenge in the absence of fur
- Changes in CR fur are necessary for thermal homeostasis and metabolic fitness
Exercise-stimulated interleukin-15 is controlled by AMPK and regulates skin metabolism and aging
Original Contribution

Occupational stress of anesthesia: Effects on aging☆

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ABSTRACT

Background: Anesthesiology has been identified as a stressful specialty. Chronic psychological stress may lead to biological aging and skin aging.

Study objective: The primary outcome was to measure physical health and emotional well-being. Secondary outcomes include skin aging analysis, telomere shortening in anesthetists.

Design: This is a prospective observational study.

Settings: University of Alexandria.

Patients: Study was carried out on 366 ASA I–II physicians 30–50 yr.

Interventions: Physicians were categorized into two equal groups, Group A (183) were anesthesia physicians and Group B (183) were physicians in less stressful specialties (laboratory specialties). Subgroup analysis was performed comparing 10 years' intervals from (30–40) and from (40–50).

Measurements: Physical health and emotional well-being were evaluated. All physicians were exposed to validated assessment scales for the upper face and the lower face for skin aging analysis. Blood sampling were drowned from all physicians during their working hours for analysis of telomere length, markers of oxidative stress.

Results: The two studied groups showed comparable demographic data and years of work. Physical health score and emotional health score showed higher values in Group A than Group B. Upper and lower face aesthetic unit summary score showed higher values in Group A than Group B. Telomere (TTAGGG) repeats for terminal restriction fragments (TRF) of Group A individuals revealed a significant decrease of TRF compared to Group B (p = 0.001*).

Conclusion: Biological and skin aging is evident in anesthetists who are chronically exposed to occupational stress, with obvious shorter telomere length, higher lower and upper face scores, and free radicals.

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### Table 2. Studies with skin aging, facial appearance and sleep.

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Ethnicity</th>
<th>Number of Subjects</th>
<th>Sleep Disorders</th>
<th>Skin Features</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oyetakin-White</td>
<td>2015</td>
<td>Caucasian</td>
<td>60 women</td>
<td>Sleep quality PSQI &gt;5, sleep duration &lt;5 h</td>
<td>Skin aging measured by SCINEXA™ and skin barrier measured by transepidermal water loss</td>
<td>Lower intrinsic aging scores in good sleepers, and 30% greater barrier function compared to poor sleepers</td>
</tr>
<tr>
<td>Sundelin</td>
<td>2013</td>
<td>Swedish</td>
<td>20 women</td>
<td>Normal sleeper and 31 h of sleep deprivation followed by 5 h of sleep</td>
<td>40 observers rated facial photographs for fatigue, facial cues and sadness</td>
<td>Sleep deprived had more swollen eyes, darker circles, more wrinkles, fine lines and more droopy corners of the eyes</td>
</tr>
<tr>
<td>Chervin</td>
<td>2013</td>
<td>USA</td>
<td>14 men and 6 women</td>
<td>OSA</td>
<td>22 raters noted post treatment patients</td>
<td>Post treatment patients appeared more alert, more youthful and more attractive</td>
</tr>
</tbody>
</table>

OSA-Obstructive Sleep Apnea, PSQI-Pittsburgh Sleep Quality Index.
Special Topic

Sleep Wrinkles: Facial Aging and Facial Distortion During Sleep

Goesel Anson, MD, FACS; Michael A.C. Kane, MD; and Val Lambros, MD, FACS