Pathogenesis & management of acne scarring
Disclosures

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Agenda

01 Background
  • Prevalence
  • Impact

02 Development of atrophic acne scars
  • Clinical
  • Basic science

03 Management
  • Prevention
  • Reduction
  • Correction
01 Background
• Prevalence
• Impact

RISK FACTORS?

02 Development of atrophic acne scars
• Clinical
• Basic science

ARE THEY PERMANENT?
DOES INFLAMMATION DIFFER?

03 Management
• Prevention
• Reduction
• Correction

EVIDENCE FOR REDUCTION?
CORRECTION?

Agenda/Controversies
Prevalence of Scarring with Acne Severity

Adapted from Tan J et al. J Drugs Dermatol 2017; 16(2):97-102

43% of all patients (n=1,972) had acne scars
Acne Scars can adversely impact Quality of Life (DLQI)

- No effect/ Mild effect (0-5)
- Moderate effect/ Very large effect (6-20)

How People with Facial Acne Scars are Perceived

Multi-national online survey (4,618 responders)

First Thing Noticed About a Person’s Face

All p<0.05

Adapted from Dréno B, et al. Dermatol Ther (Heidelb) 2016;6(2):207–218
How People with Facial Acne Scars are Perceived

<table>
<thead>
<tr>
<th>Traits of Individuals</th>
<th>Acne Scars (%) (n=6956 pictures)</th>
<th>Clear skin (%) (n=6898 pictures)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attractive</td>
<td>17</td>
<td>25</td>
</tr>
<tr>
<td>Confident</td>
<td>25</td>
<td>33</td>
</tr>
<tr>
<td>Healthy</td>
<td>21</td>
<td>31</td>
</tr>
<tr>
<td><strong>Skills of Individual</strong></td>
<td><strong>Public speaking</strong></td>
<td><strong>Sports</strong></td>
</tr>
<tr>
<td></td>
<td>24</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>23</td>
<td>27</td>
</tr>
<tr>
<td><strong>Impact on Individual’s Life</strong></td>
<td><strong>Stressed</strong></td>
<td><strong>Make people uncomfortable</strong></td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>30</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>24</td>
</tr>
</tbody>
</table>

All p<0.05

Adapted from Dréno B, et al. Dermatol Ther (Heidelb) 2016;6(2):207–218
## Risk Factors for Acne Scars

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>CATEGORY THRESHOLDS</th>
<th>ODDS RATIOS [CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity of acne</td>
<td>Severe-very severe vs. Almost clear-moderate</td>
<td>3.68 [2.58–5.23]</td>
</tr>
<tr>
<td>Family history of acne scarring</td>
<td>Yes vs. No</td>
<td>2.14 [1.67–2.76]</td>
</tr>
<tr>
<td>Duration of acne</td>
<td>1 year or more vs. 1 year or less</td>
<td>1.63 [1.09–2.47]</td>
</tr>
<tr>
<td>Squeezing and picking behaviours</td>
<td>Frequently – all the time vs. Never – sometimes</td>
<td>1.70 [1.27–2.29]</td>
</tr>
</tbody>
</table>

Atrophic acne scar formation from primary acne lesions

6 month observational study of moderate inflammatory acne with digitized facial mapping

36% of scars disappeared at 6 months

Ongoing acne scar formation & repair

Immune Responses in Patients Prone to Scarring

Atrophic Acne Scar Management

I. Prevention
Premise

No acne

No acne scars
Atrophic Acne Scar Management

II. Mitigation
Delay to effective acne treatment correlates with scar prevalence

Isotretinoin for Prevention of Acne Scarring

**Design**
- Prospective clinical study
- Moderate to severe acne (n=107)

**Study Treatment**
- Once daily, isotretinoin 1 mg/kg/day for 4 months (cumulative dose of 120 mg/kg)

Earlier treatment with isotretinoin reduced scar severity

Matrix Repair Capability of Tretinoin *in vitro*

*P. acnes* induces MMP-9 and TIMP in human monocytes.

Tretinoin modulates MMP-9/TIMP expression, shifting from a matrix-degradative phenotype to a matrix-preserving phenotype.

Treatment of monocytes with tretinoin (all-trans retinoic acid) inhibits MMP-9 and augments TIMP-1 expression.

Adapalene 0.3% Gel Improves Skin Texture and Appearance of Atrophic Acne Scars

• **Design**
  • 24-week, open-label study (n=20)
  • Patients with past history of acne (no active lesions at time of enrollment)
  • Moderate to severe facial atrophic acne scars
    • Grade 3 or 4* and ≥5 atrophic scars

• **Study Treatments**
  • Adapalene 0.3% once daily for first 4 weeks, then twice daily for 20 weeks
  • Daily skin care: Skin cleanser, moisturizing lotion and SPF50 sunscreen

Adapalene 0.3% Gel: Improvement in scar severity

IGA, Investigator’s Global Assessment; Adapted from Loss MJ et al. *Dermatol Ther (Heidel)*. 2018 Jun;8(2):245-257
Increased

• Procollagen-1 by 15%
• Collagen-3 by 58%

Enhanced Collagen Synthesis with Adapalene 0.3%

Adapalene 0.1%/BPO 2.5% Split-Face Study

• **Design**
  • 6-month split-face, investigator-blinded, vehicle-controlled study
  • Randomized controlled trial
  • Moderate facial acne
  • ≥10 atrophic acne scars at baseline (n=31)

A0.1/BPO2.5, adapalene 0.1%/benzoyl peroxide 2.5%; J Eur Acad Dermatol Venereol. 2017 Apr;31(4):737-742
A0.1%/BPO 2.5% Reduces Risk of Atrophic Scars and Improves Scar Severity

\[ p = 0.036 \]

Mean scar count

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle</td>
<td>10.9</td>
<td>13.6</td>
</tr>
<tr>
<td>A/BPO</td>
<td>11.1</td>
<td>11.6</td>
</tr>
</tbody>
</table>

\[ p = 0.0032 \]

% almost clear (SGA)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle</td>
<td>9.7</td>
<td>6.5</td>
</tr>
<tr>
<td>A/BPO</td>
<td>9.7</td>
<td>45.2</td>
</tr>
</tbody>
</table>
Adapalene 0.3%/BPO 2.5% Gel in acne and acne scarring (OSCAR Study)

- **Design**
- 24-week split-face, investigator-blinded, vehicle-controlled study
- Moderate to severe facial acne (n=67)

Once daily 
A0.3/BPO2.5 gel

Acne Global Success (%IGA clear/almost clear)

A0.3/BPO2.5, adapalene 0.3% / benzoyl peroxide 2.5%; IGA, Investigator Global Assessment

Acne Scar Results

Atrophic Scar Count Change from Baseline

*\( p<0.001; \quad **p<0.0001 \)

A0.3/BPO2.5, adapalene 0.3%/ benzoyl peroxide 2.5%; SGA, Scar Global Assessment; Adapted from Dréno B et al. *Am J Clin Dermatol.* 2018 Epub ahead of print
Atrophic Acne Scar Management

III. Correction/Repair
Patients present with multiple types of acne scars
Types of Atrophic Acne Scars

- **Icepick**
- **Rolling**
- **Boxcar**
- **Super Boxcar >4 mm**

Tethering by scar tissue under all scar types

### Scar Type | Treatment Modalities
---|---
Ice pick | Chemical peel (CROSS technique), punch techniques, RF
Boxcar | Dermabrasion (shallow), dermal fillers (shallow), lasers (ablative, nonablative, fractional; shallow), punch techniques (deeps), RF (shallow, deep), skin needling (shallow), subcision (shallow)
Rolling | Dermabrasion, dermal fillers, lasers (ablative, nonablative, fractional), RF, skin needling, subcision

RF, radiofrequency; CROSS, chemical reconstruction of skin scars; PDL, pulsed dye laser; Lanoue J and Goldenberg G *Cutis*. 2015;95:276-281.
# Effectiveness of Correction Procedures for Acne Scarring

<table>
<thead>
<tr>
<th>Modality</th>
<th>Ice Pick Scars</th>
<th>Boxcar Scars</th>
<th>Rolling Scars</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemical Peels</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TCA CROSS technique</td>
<td>++</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td><strong>Dermabrasion/microdermabrasion</strong></td>
<td>+</td>
<td>+</td>
<td>-</td>
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<tr>
<td><strong>Laser</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ablative and nonablative laser</td>
<td>-</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Fractional laser photothermolysis</td>
<td>++</td>
<td>++</td>
<td>++</td>
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<tr>
<td><strong>Punch Techniques</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Punch excision</td>
<td>++</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Punch elevation</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Punch replacement grafting</td>
<td>++</td>
<td>-</td>
<td>-</td>
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<tr>
<td><strong>Tissue augmenting agents</strong></td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Needling</td>
<td>-</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Subcision</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
</tbody>
</table>

++ = effective, + = less effect, - = not effective

Atrophic Acne Scar Algorithm

Atrophic Acne Scars

Topical retinoids
Peels (GA, TCA, Phenol)

Ice Pick
• TCA CROSS
• Punch excision

Boxcar
• TCA CROSS
• Lasers: ablative & non-ablative
• Microneedling ± PRP
• RF: microneedle or fractional bipolar
• Dermabrasion
• Punch elevation

Rolling
• Subcision
• Lasers: ablative & non-ablative
• Microneedling ± PRP
• RF: microneedle or fractional bipolar
• Fillers

KEY:
TCA CROSS: trichloroacetic acid chemical reconstruction of skin scars; PRP, platelet-rich plasma; RF: radiofrequency

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EVIDENCE FOR REDUCTION?
CORRECTION?
Modifiable risk factors in scarring – duration, severity, manipulation

Scarring results from intensity and duration of inflammation; inadequate matrix repair

Atrophic acne scars can repair spontaneously

Topical retinoids can reduce scar formation

Acne scarring can be reduced and corrected

Key Messages: Atrophic acne scarring