Treating Acne in Women
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DISCLOSURE OF RELEVANT RELATIONSHIPS WITH INDUSTRY

Bethanee J. Schlosser, MD, PhD
S007: Acne and Rosacea
Treating Acne in Women
Author: UpToDate®
Advisory Board: Allergan, UCB, Beiersdorf
Speaker: Allergan

Off-label use of medication will be discussed.
• Epidemiology of acne in adults

• Sex differences in efficacy of acne therapy
  – Topical therapies
  – Oral isotretinoin

• Spironolactone for acne in adult women
  – Predictors of response
  – Serum potassium monitoring
Epidemiology of Acne in Adults
Adult Acne Affects More Women than Men

- Survey study of university campus
- 1013 adults ages 20 and older

Acne in Adult Women

- 2895 women ages 10-70
- Photographs for acne, scars, dyschromia
- Sebum, pore size measurements

<table>
<thead>
<tr>
<th>Overall Prevalence of Clinical Acne</th>
<th>26.7%</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-30yo</td>
<td>45%</td>
</tr>
<tr>
<td>31-40yo</td>
<td>26%</td>
</tr>
<tr>
<td>41-50yo</td>
<td>12%</td>
</tr>
</tbody>
</table>

Sex Differences in Efficacy of Acne Therapy
Topical Acne Treatment Response by Sex

- Post-hoc analysis of phase 3 RCT, moderate to severe acne
- Clindamycin 1.2%/BP 3.75% gel QD vs vehicle

<table>
<thead>
<tr>
<th></th>
<th>Vehicle Female</th>
<th>Vehicle Male</th>
<th>Clinda/BPO Female</th>
<th>Clinda/BPO Male</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean reduction -</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory</td>
<td>30.3%</td>
<td>32.3%</td>
<td>65.3%</td>
<td>55.8%</td>
<td>0.049</td>
</tr>
<tr>
<td>Mean reduction -</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noninflammatory</td>
<td>30.2%</td>
<td>25.2%</td>
<td>55.7%</td>
<td>48.1%</td>
<td>0.084</td>
</tr>
<tr>
<td>≥ 2 grades improvement</td>
<td>20.5%</td>
<td>13.6%</td>
<td>42.5%</td>
<td>28.2%</td>
<td>0.049</td>
</tr>
</tbody>
</table>

Topical Acne Treatment Response by Sex

- Dapsone 5% gel BID phase 3 pooled data analysis
- N=2898, moderate inflammatory acne
- Baseline lesion counts: M 84.10 vs F 74.05 dapsone group

<table>
<thead>
<tr>
<th></th>
<th>Vehicle Female</th>
<th>Vehicle Male</th>
<th>Dapsone 5% Female</th>
<th>Dapsone 5% Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lesion counts</td>
<td></td>
<td></td>
<td>46.6%</td>
<td>35.8% (p&lt;0.0001)</td>
</tr>
<tr>
<td>Mean reduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noninflammatory</td>
<td></td>
<td></td>
<td>39.8%</td>
<td>28.5% (p&lt;0.0001)</td>
</tr>
<tr>
<td>Mean reduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory</td>
<td></td>
<td></td>
<td>56.8%</td>
<td>43.2% (p&lt;0.0001)</td>
</tr>
<tr>
<td>Mean reduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear/almost clear</td>
<td>39.4%</td>
<td>28.0% (p 0.0013)</td>
<td>48.6%</td>
<td>34.4% (p 0.0003)</td>
</tr>
</tbody>
</table>

## Topical Acne Treatment Response by Sex

- Dapsone 7.5% gel QD, phase 3, pooled subgroup analysis
- N=4340, moderate inflammatory acne

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<th>Dapsone 7.5% Female</th>
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<tbody>
<tr>
<td>Total lesion counts</td>
<td>45.8%</td>
<td>39.7%</td>
<td>53.4%</td>
<td>44.2%</td>
</tr>
<tr>
<td>Mean reduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Noninflammatory</td>
<td>37.1%</td>
<td>41.8%</td>
<td>49.8%</td>
<td>40.3%</td>
</tr>
<tr>
<td>Mean reduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammatory</td>
<td>44.3%</td>
<td>51.9%</td>
<td>49.7%</td>
<td>59.5%</td>
</tr>
<tr>
<td>Mean reduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clear/almost clear</td>
<td>23.2%</td>
<td>18.3%</td>
<td>33.9%</td>
<td>24.7%</td>
</tr>
</tbody>
</table>

Adult Female Acne and Isotretinoin

- Retrospective review of 405 pts
- Status-post isotretinoin ≥ 150mg/kg total dose
- 72.1% female, 71.6% > 20yo, 80.9% relapse within 2 yr

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Relapse Incidence (further medical tx)</th>
<th>2nd Course of Isotretinoin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>72/292 (24.6%)</td>
<td>24/72 (33.3%)</td>
</tr>
<tr>
<td>Males</td>
<td>22/113 (19.5%)</td>
<td>7/22 (31.8%)</td>
</tr>
<tr>
<td>Age &lt; 20yo</td>
<td>27/115 (23.5%)</td>
<td>4/27 (14.8%)</td>
</tr>
<tr>
<td>Age ≥ 20yo</td>
<td>67/290 (23.1%)</td>
<td>27/67 (40.3%)</td>
</tr>
</tbody>
</table>

- Hormonal therapy was not part of regimen

Adult Female Acne and Isotretinoin

- Stainforth et al\(^1\)
  - 299 patients, followed 5 years post-isotretinoin
  - Risk factors: female > 25yo, persistent acne

- Coloe et al\(^2\)
  - 102 patients, followed ≥ 1 year
  - 16 retrial of isotretinoin
  - Mean cumulative dose by weight (mg/kg): 268.69 vs 216.72 (p 0.009)
  - Isotretinoin retrial for F vs M: OR 4.109 (p 0.018)

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Spironolactone for Acne

- 85 adult women
- 79% failed oral antibiotic
- 14% failed isotretinoin
- 50-100mg/day
- Mean duration = 10 months

Predicting Response to Spironolactone

- Retrospective, 70 F ≥ 20yo (mean 31.3yo) with facial acne
- Spironolactone ≤ 150mg/day x median 6 months
- Remission = ≤ 5 comedones, ≤ 2 inflammatory
- 75% prior OCP; 56% prior isotretinoin

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>High # inflammatory lesions at inclusion</td>
<td>1.08 (1.03-1.13)</td>
<td>0.001</td>
</tr>
<tr>
<td>Relapse with previous isotretinoin</td>
<td>2.46 (1.09-5.54)</td>
<td>0.029</td>
</tr>
<tr>
<td>OCP containing 1st or 2nd generation progestin</td>
<td>2.77 (1.35-5.71)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Monitor serum potassium within 1 week of initiation or titration of ALDACTONE and regularly thereafter. More frequent monitoring may be needed when ALDACTONE is given with other drugs that cause hyperkalemia or in patients with impaired renal function.

- CHF
- HTN
- Edema
- Primary hyperaldosteronism
Serum [K]: No Need to Monitor in Healthy Young Acne Patients

- Retrospective study, 2000-2014
- 967 healthy women, 18-45yr
- Mean age = 27.5yr and 26.2yr

- Baseline ↑ [K] = 0.76%
- +Spironolactone ↑ [K] = 0.72% (13/1802)

- Dose, duration of spironolactone

Serum [K]: Monitor in Older Acne Patients

- Retrospective study, 2006-2016
- 618 women ages 18-65yo prescribed spironolactone for acne
- 124 serum [K] at baseline and at follow-up within 12 months
  - No comorbidities of interest (HTN, DM, renal failure)
  - Mean age at spironolactone initiation = 32yo (18-57yo)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>N</th>
<th>Rate of Incident Hyperkalemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-45yo</td>
<td>112</td>
<td>1 (0.9%)</td>
</tr>
<tr>
<td>46-65yo</td>
<td>12</td>
<td>2 (16.7%)</td>
</tr>
</tbody>
</table>

- p = 0.0245

Serum [K] Monitoring Guidelines

- Renal function, electrolytes
  - Older patients (>45yo)
  - Higher doses of spironolactone (200mg/day)
  - History of renal or cardiac disease
  - Concomitants medications which may influence renal function or serum [K]

- ROS: dizziness, lethargy, abnormal thirst, muscle cramps, ↑ HR, ↓ urination
Take Home Points

- Acne disproportionately affects adult women for longer durations.
- Some topical acne therapies exhibit sex differences in efficacy.
- Adult females are at greater risk of acne relapse following isotretinoin therapy.
- Serum potassium monitoring should be considered in older women taking spironolactone for acne.