Oral Therapy Debate: Antibiotics

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Disclosures

Allergan  Crown
Procter and Gamble  Evolus
L’Oreal  Cassiopea
Ortho Derm  Ferndale
Aclaris  Regimen Pro
Revance  CLN
Sonoma  Almirall
Antibiotics for Acne

- Tetracyclines (minocycline, doxycycline) - 1st Line
- Macrolides
- Trimethoprim/ Sulfamethoxazole
- Topicals: Clindamycin, erythromycin

Propionibacterium acnes

- Gram positive anaerobic diphtheroid
- Low pathogenicity
- Levels elevated in acne patients
- Hypersensitivity may explain variability of clinical presentation
- Generates inflammation
  - FFA hypothesis
  - Complement
  - Neutrophil chemotactic factor
  - Enhanced lymphocytic response
Tetracyclines

- Antibacterial – inhibit bacterial protein synthesis
- Anti-inflammatory – inhibit:
  - Neutrophil chemotaxis
  - Cytokine production (IL-8, TNF-alpha)
  - Macrophage function
  - Neutrophil release ROS
  - MMP’s

Minocycline

- FDA approved extended release 1mg/kg
- Lipophilic, least resistance
- Side effects: Vestibular, pigment, LE syndrome, hepatic, pseudotumor cerebri
Doxycycline

- **Side effects:**
  - GI, esophagitis, candidiasis, photosensitivity, ? IBD
- **Sub antimicrobial:**
  - ↓ effect on oropharynx, GI, skin, vaginal flora

*RESISTANCE*

Erythromycin > Clindamycin > TCN > Doxycycline > Minocycline

- Can be transmitted to personal contacts
Systemic Antibiotics – Antibiotic Stewardship

- Minocycline, doxycycline
- Limit 3-6 months
- Use with topical BP
- Avoid topical antibiotic monotherapy
- Topicals for maintenance

Microbiome

- Layer of living organisms that coat skin surface
- Component of epidermal barrier
- Bacteria, Fungi, yeast
- Diverse – mostly commensal organisms
  - bacteria, secrete antimicrobial peptides
  - regulate immune system and promote immune tolerance
  - maintain low skin PH
- Dysbiosis (microbiome alteration) in patients with acne
- Microbiome “friendly” skin care
  - doesn't disturb microbiome
  - modulate to improve barrier repair and decrease inflammation
**Broad-spectrum: Oral Minocycline**

**Conclusion:** Minocycline produces significant derangements in the microbiota of the skin and gut, including many probiotic species, highlighting the potential for more targeted antimicrobial treatments for acne.

**Broad-spectrum: Oral Doxycycline**

**Clinical Research: Epidemiology of Skin Diseases**

383 Doxycycline effects on the gut and skin microbiomes and lipidome in acne

K. Haas 1, M. Notay 3, W. Rodriguez 2, M. Rolston 1, A. Clark 1, W. Burney 1, J. Newman 1, T. Pedersen 1, R. Crawford 3, S. Dandekar 1, R. Sivamani 1
Potential Association Between the Oral Tetracycline Class of Antimicrobials Used to Treat Acne and Inflammatory Bowel Disease

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Association of doxycycline use with the development of gastroenteritis, irritable bowel syndrome and inflammatory bowel disease in Australians deployed abroad

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Sarecycline: Modified Structure to Overcome Resistance Mechanism

Sarecycline has the longest C7-moiety present in any tetracycline-class drug

The position marked in orange at C-7 has been modified to create tetracycline derivatives to overcome tetracycline resistance mechanisms and to change bacterial ribosome binding

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C7 Position Modification
overcomes efflux pump

Broad Spectrum Antibiotics:
- Tetracycline, Doxycycline, Minocycline
  - Inhibit many types of bacteria throughout the body

Narrow Spectrum Antibiotics:
- Sarecycline
  - Inhibit a limited number of bacteria in specific locations

References:

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Due to concerns regarding antimicrobial resistance, the Centers for Disease Control and Prevention (CDC) has stressed antibiotic stewardship. This is an initiative to promote the appropriate use of antibiotics where patients receive the right dose of the right antibiotic at the right time for the right duration.

"Core principles of antibiotic stewardship include selecting narrow-spectrum agents when feasible, using antibiotics only when necessary, and prescribing antibiotics for the shortest effective duration,"

Source: https://www.cdc.gov/hrp/antibiotic-stewardship/nurse-who-use.html

"and facilitate use of narrow-spectrum antibiotics whenever possible" – CDC

Source: Antibiotic Stewardship Statement for Antibiotic Guidelines – Recommendations of the HICPAC

"Promoting narrow-spectrum over broad-spectrum antibiotic use is a common goal of stewardship programs."

Daniel Livorsi, MD, MSc