Controversies in Oral Therapy for Acne

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Disclosures

IN DR. DEL ROSSO'S ACNE

& ROSACEA LECTURE LIKE...

* Research Investigator
^ Consultant/Advisor
# Speaker

INCYTE*
LEO PHARMA**^#
LA ROCHE POSAY^
MC2^
MENLO THERAPEUTICS**^#
NOVAN^*
ORTHO DERMATOLOGY**^#
PFIZER^#
RALEXAR*
REGENERON**^#
SANOFI-GENZYME^#
SKINFIX^*
SOLGEL^*
SONOMA (INTRADERM)^*
SUN PHARMA**^#
VERRICA^*

UPDATED 01-23-2020
• **Controversy** is a state of prolonged public dispute or debate, usually concerning a matter of opinion. The word was coined from the Latin **controversia**, as a composite of **controversus** – "turned in an opposite direction," from **contra** – "against" – and **vertere** – to turn, or **versus** (see **verse**), hence, "to turn against."
Controversies in Oral Therapy for Acne

MAJOR CONTROVERSY RELATES TO
ANTIBIOTIC RESISTANCE CONCERNS
→ MICROBIOME CHANGES

MAJOR CONTROVERSIES RELATE TO
SAFETY CONSIDERATIONS?
WHO IS A CANDIDATE FOR THERAPY?
DOSING REGIMEN?
POTENTIAL FOR RELAPSE?

MAJOR CONTROVERSY RELATES TO
LABORATORY MONITORING
### Therapeutic Options for Moderate to Severe Acne

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination therapy</td>
<td>Oral antibiotics + topical retinoids ± BPO</td>
</tr>
<tr>
<td></td>
<td>First line</td>
</tr>
<tr>
<td>Hormonal therapy</td>
<td>Women with moderate to severe acne, especially if contraception is desirable</td>
</tr>
<tr>
<td></td>
<td>Used in combination with other modalities</td>
</tr>
<tr>
<td>Isotretinoin</td>
<td>Severe and/or recalcitrant acne</td>
</tr>
<tr>
<td></td>
<td>Teratogenic; stringently regulated for women with childbearing potential</td>
</tr>
</tbody>
</table>

### Acne Treatment Algorithm

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Comedonal</strong></td>
<td>Topical retinoid</td>
<td>Topical retinoid</td>
<td>Oral antibiotic</td>
</tr>
<tr>
<td><strong>Papular/pustular</strong></td>
<td>+ topical antimicrobial</td>
<td>+ topical retinoid</td>
<td>+ topical retinoid</td>
</tr>
<tr>
<td><strong>Papular/pustular</strong></td>
<td>Oral antibiotic</td>
<td>Oral antibiotic</td>
<td>Oral isotretinoin</td>
</tr>
<tr>
<td><strong>Nodular</strong></td>
<td>Oral antibiotic</td>
<td>Oral antibiotic</td>
<td>Oral isotretinoin</td>
</tr>
<tr>
<td><strong>Nodular/conglobate</strong></td>
<td>Oral isotretinoin</td>
<td>Oral isotretinoin</td>
<td>High-dose oral antibiotic</td>
</tr>
</tbody>
</table>

#### First Choice
- Topical retinoid
- Azelaic acid or salicylic acid
- See first choice
- Topical retinoid

#### Alternatives
- Topical retinoid + topical antimicrobial
- Alt. topical antimicrobial agent + alt. topical retinoid or azelaic acid
- Oral anti-androgen
- Oral anti-androgen

#### Alternatives for Females
- High-dose oral anti-androgen
- Topical retinoid + BPO
- Topical retinoid + BPO

#### Maintenance Therapy
- Topical retinoid
- Topical retinoid + BPO

Status Report from the Scientific Panel on Antibiotic Use in Dermatology of the American Acne and Rosacea Society

Part 1: Antibiotic Prescribing Patterns, Sources of Antibiotic Exposure, Antibiotic Consumption and Emergence of Antibiotic Resistance, Impact of Alterations in Antibiotic Prescribing, and Clinical Sequelae of Antibiotic Use

*JAMES Q. DEL ROSSO, DO; GUY F. WEBSTER, MD; TED ROSEN, MD; DIANE THIBOUTOT, MD; JAMES J. LEYDEN, MD; RICHARD GALLO, MD, PhD; CLAY WALKER, PhD; GEORGE ZHANEL, PhD; LAWRENCE EICHENFIELD, MD

Department of Dermatology, Jefferson Medical College, Philadelphia, Pennsylvania; Department of Dermatology, Baylor College of Medicine, Houston, Texas; Department of Dermatology, University of California San Diego, San Diego, California; University of Florida Dental School, Gainesville, Florida; Department of Dermatology, University of Manitoba, Winnipeg, Canada; Department of Dermatology, University of California San Diego, San Diego, California.

ABSTRACT

Oral and topical antibiotics are commonly prescribed in dermatologic practice, often for noninfectious disorders, such as acne vulgaris and rosacea. Concerns related to antibiotic exposure from both medical and nonmedical sources require that clinicians consider in each case why and how antibiotics are being used and to make appropriate adjustments to limit antibiotic exposure whenever possible. This first article of a three-part series discusses prescribing patterns in dermatology, provides an overview of sources of antibiotic exposure, reviews the relative correlations between the magnitude of antibiotic consumption and emergence of antibiotic resistance patterns, evaluates the impact of alterations in antibiotic prescribing, and discusses the potential relevance and clinical sequelae of antibiotic use, with emphasis on how antibiotics are used in dermatology. (J Clin Aesthet Dermatol. 2016;9(4):18-24.)
Acne and Antibiotics

Arguments against their use:
- Increases in antibiotic-resistant Corynebacterium acnes strains
- Increase in antibiotic-resistant commensal and opportunistic bacteria

Arguments for their use:
- Creates antibiotic resistance
- Moderate efficacy
- Temporary results
- Creates drug-resistant bacteria
- Many side effects

Antibiotic Resistance
Clinical Expectations: Combination Therapy With an Oral Antibiotic

- Aggressive initial therapy
  - Resolves lesions
  - Prevents scarring
- Inflammatory acne often resolves within 1 to 3 months
- Then move to less aggressive regimen

Oral Antibiotics Used to Treat Moderate to Severe Acne

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline</td>
<td>First-line agents</td>
</tr>
<tr>
<td>Minocycline</td>
<td></td>
</tr>
<tr>
<td>Lymecycline</td>
<td>Not approved in the United States</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Slower response than second-generation tetracyclines</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Resistance is highly prevalent</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>Used where tetracyclines are contraindicated or not tolerated</td>
</tr>
<tr>
<td>Trimethoprim</td>
<td>Third line; used for acne resistant to tetracyclines and macrolides</td>
</tr>
</tbody>
</table>

What's New!!!
Efficacy and Safety of Sarecycline, a Novel, Once-Daily, Narrow Spectrum Antibiotic for the Treatment of Moderate to Severe Facial Acne Vulgaris: Results of a Phase 2, Dose-Ranging Study.

Leyden JJ, Sniukene V, Berk DR, Kaoukhov A.

Abstract

BACKGROUND: There is a need for new oral antibiotics for acne with improved safety profiles and targeted antibacterial spectra. Sarecycline is a novel, tetracycline-class antibiotic specifically designed for acne, offering a narrow spectrum of activity compared with currently available tetracyclines, including less activity against enteric Gram-negative bacteria. This phase 2 study evaluated the efficacy and safety of three doses of sarecycline for moderate to severe facial acne vulgaris.

METHODS: In this multicenter, double-blind, placebo-controlled study, patients aged 12 to 45 years were randomized to once-daily sarecycline 0.75 mg/kg, 1.5 mg/kg, 3.0 mg/kg, or placebo. Efficacy analyses included change from baseline in inflammatory and noninflammatory lesion counts at week 12, with between-group comparisons using analysis of covariance. Safety assessments included adverse events (AEs), clinical laboratories, vital signs, electrocardiograms, and physical examinations.

RESULTS: Overall, 285 randomized patients received at least one dose of study drug. At week 12, sarecycline 1.5 mg/kg and 3.0 mg/kg groups demonstrated significantly reduced inflammatory lesions from baseline (52.7% and 51.8%, respectively) versus placebo (38.3%; P=0.02 and P=0.03, respectively). Sarecycline was safe and well tolerated, with similar gastrointestinal AE rates in sarecycline and placebo groups. Vertigo and photosensitivity AEs occurred in less than 1% of patients when pooling sarecycline groups; no vulvovaginal candidiasis AEs occurred. Discontinuation rates due to AEs were low. No serious AEs occurred.

CONCLUSION: Once-daily sarecycline 1.5 mg/kg significantly reduced inflammatory lesions versus placebo and was safe and well tolerated with low rates of AEs, including gastrointestinal AEs. Sarecycline 3.0 mg/kg did not result in additional efficacy versus 1.5 mg/kg. Sarecycline may represent a novel, once-daily treatment for patients with moderate to severe acne. It offers a narrow antibacterial spectrum relative to other tetracycline options, which may lead to less selective pressure on enteric Gram-negative bacteria, resulting in less disruption of commensal organisms and less potential for antibiotic resistance. <p>&lt;em&gt;J Drugs Dermatol. 2018;17(3):333-338.&lt;/em&gt;&lt;/p&gt;
Sarecycline vs Placebo in Acne Vulgaris
Inflammatory Lesion Count Reduction (%)

Sarecycline 1.5 mg/kg/day QD (n=1002) vs Placebo – 12-Weeks
Age Range 9-45 Years / ~25% Non-White Skin / 85% Moderate Severity

Mean Percent Change in Inflammatory Lesion Count from Baseline to Week 12

- Mean absolute reduction in lesion count was statistically significant at Week 12 and as early as Week 3


MAY BE TAKEN WITH OR WITHOUT FOOD
Sarecycline vs Placebo in Truncal Acne Vulgaris

Sarecycline 1.5 mg/kg/day Once Daily (n=1002) vs Placebo – 12-Weeks
Age Range 9-45 Years / ~25% Non-White Skin / 85% Moderate Severity

Proportion of Subjects with Non-facial IGA Success at Week 12

Non-facial IGA success defined as a ≥2-point decrease from baseline and a score of clear/almost clear
Sarecycline Once Daily in Acne Vulgaris
Global Assessment and Inflammatory Lesion Count Improvements

Baseline
Severe
WEEK 12
Almost Clear

92% lesion reduction from baseline

76% lesion reduction from baseline
Practical Considerations with Sarecycline
Concept of Narrow Spectrum Tetracycline

POTENTIAL CONSIDERATIONS RELEVANT TO CLINICAL PRACTICE

EFFICACY FOR ACNE VULGARIS
Inflammatory AND Comedonal Lesions Face & Trunk

ADVERSE REACTION PROFILE
GI Side Effects / Photosensitivity / Vaginal Candidiasis

ANTIMICROBIAL SPECTRUM
Reduced Risk of Antibiotic Resistance vs Some Organisms (especially Gram - )

REDUCE SELECTION OF GRAM (-) BACTERIA AND MULTI-DRUG RESISTANCE
Microbiological Profile of Sarvecycline, a Novel Targeted Spectrum Tetracycline for the Treatment of Acne Vulgaris.

Zhanel G¹, Critchley P², Lin LY³, Alvandi N².

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2 Allergan plc, Irvine, California, USA.
3 Allergan plc, Irvine, California, USA Lin_Lynn-Yao@Allergan.com.

Abstract
Sarvecycline is the first narrow-spectrum tetracycline-class antibiotic being developed for acne treatment. In addition to exhibiting activity against important skin/soft tissue pathogens, sarvecycline exhibits targeted antibacterial activity against clinical isolates of Cutibacterum acnes. In the current study, sarvecycline was 16- to 32-fold less active than broad-spectrum tetracyclines such as minocycline and doxycycline against aerobic Gram-negative bacilli associated with the normal human intestinal microbiome. Also, reduced activity against Escherichia coli was observed in vivo in a murine septicemia model, with the 50% protective doses, or the doses required to achieve 50% survival, being >40 mg/kg of body weight and 5.72 mg/kg for sarvecycline and doxycycline, respectively. Sarvecycline was also 4- to 8-fold less active than doxycycline against representative anaerobic bacteria that also comprise the normal human intestinal microbiome. Additionally, C. acnes strains displayed a low propensity for the development of resistance to sarvecycline, with spontaneous mutation frequencies being $10^{-10}$ at 4 to 8 times the MIC, similar to those for minocycline and vancomycin. When tested against Gram-positive pathogens with defined tetracycline resistance mechanisms, sarvecycline was more active than tetracycline against tet(K) and tet(M) strains, with MICs ranging from 0.125 to 1.0 µg/ml and 8 µg/ml, respectively, compared with MICs of 16 to 64 µg/ml and 64 µg/ml for tetracycline, respectively. However, sarvecycline activity against the tet(K) and tet(M) strains was decreased compared to that against the wild type, which demonstrated MICs ranging from 0.06 to 0.25 µg/ml, though the decrease in the activity of sarvecycline against the tet(K) and tet(M) strains was not as pronounced as that of tetracycline. These findings support sarvecycline as a narrow-spectrum tetracycline-class antibiotic that is effective for the treatment of acne, and further investigation into the potential reduced effects on the gut microbiome compared with those of other agents is warranted.

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**Sarecycline in Acne Vulgaris: Pooled Safety Data**

**Sarecycline 1.5 mg/kg/day Once Daily vs Placebo – 12-Weeks**

**MAJOR ADVERSE REACTIONS OF SPECIAL INTEREST WITH TETRACYCLINES**

<table>
<thead>
<tr>
<th>Effect Category</th>
<th>Condition</th>
<th>Sarecycline (%)</th>
<th>Placebo (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vestibular effects</td>
<td>Dizziness</td>
<td>0.5%</td>
<td>1.1%</td>
</tr>
<tr>
<td></td>
<td>Vertigo</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tinnitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phototoxic effects</td>
<td>Sunburn</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Photosensitivity</td>
<td>0.1%</td>
<td></td>
</tr>
<tr>
<td>Vaginal yeast infections in females</td>
<td>Vulvovaginal candidiasis(^2)</td>
<td>0.1%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Vulvovaginal mycotic infection(^2)</td>
<td></td>
<td>0.9%</td>
</tr>
</tbody>
</table>

*<1%*
Multiple Unit Particulate Pellet System (MUPS)

- Multi-particulate solid dosage form
- Compressed mixture of drug-containing pellets and powder excipients
- Can “dial in” delivery characteristics

REPORTED BENEFITS OF MUPS

- Minimizes inter/intra subject variability
- Reduces esophageal transit time
- Improves physicochemical stability
- Lowers risk of local irritation and toxicity
- Reduces dose dumping
- Minimizes plasma concentration fluctuations

Minocycline Biphasic Delivery with immediate- and sustained-release pellets.

- 25% immediate and 75% sustained release of minocycline hydrochloride
- Steady-state plasma concentration
- Functionally scored tablet has an even distribution of drug on each side of the score line
- A spherical core coated with *micronized minocycline hydrochloride*

Less Variable and More Predictable PK Profile with Minocycline Biphasic Delivery vs Biphasic Minocycline
A continued work in progress
  • Most data available with tetracyclines – “dual mechanisms”

Use in combination with *maximized topical regimen*
  • Incorporate benzoyl peroxide AND topical retinoid in regimen

AVOID antibiotic monotherapy or “unopposed” antibiotic use

Limit duration of oral antibiotic therapy *as best as possible*
  • Assess every 3 months
  • “Maximum” suggested (“hoped for”) duration: 3 - 6 months
  • Consensus agreement: “…a subset of patients for whom alternative therapies are inappropriate and who may require a longer course of antibiotics even while taking topical medications.”

The role of isotretinoin in acne therapy: why not as first-line therapy? facts and controversies.

Rigopoulos D, Larios G, Katsambas AD.

Source
Department of Dermatology, University of Athens, Andreas Sygros Hospital, 5 Ionos Dragoumi St, 16121 Athens, Greece. drigop@hol.gr

Abstract
Acne is one of the most prevalent diseases in dermatology. Millions of people worldwide experience this distressing condition. To determine the appropriate therapeutic strategy, there is a strong need for a standardized classification system of acne. The exact molecular mechanism of action of isotretinoin is not completely understood; however, oral isotretinoin targets simultaneously at all major mechanisms of acne pathogenesis. Various mass media reports about the risk of teratogenicity and depression from isotretinoin usage as well as the creation of intense prevention programs have created an obstacle to the use of the most active available drug against acne, presenting isotretinoin as a very dangerous regimen. According to recommendations of several international experts, which we share, oral isotretinoin may be prescribed not only to patients with severe disease but indications should be broadened to also include patients with less severe forms of acne, especially in cases with scarring, significant psychologic stress, or failure to respond to conventional therapy.

Oral Isotretinoin Clinical Studies
Daily Dose and Reported Relapse Rates

- Cunliffe WJ, Norris JFB. Dermatologica. 1987;175(Suppl 1):133–137;
Oral Isotretinoin Reported Relapse and Retreatment Rates

Table 1. Studies evaluating relapse of acne vulgaris after an initial course of oral isotretinoin

<table>
<thead>
<tr>
<th>Publication</th>
<th>N</th>
<th>Comparison (mg/kg/day)</th>
<th>Treatment length and follow up</th>
<th>Study results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jones DH, King K, Miller AJ, Cunliffe WJ, Br J Dermatol. 1983;108(3):333–343</td>
<td>76</td>
<td>0.1mg/kg 0.5mg/kg 1.0mg/kg</td>
<td>16 weeks treatment 16-week follow up</td>
<td>1mg/kg dose had more treatment failures and relapses—46% vs. 27–33%</td>
</tr>
<tr>
<td>Sturnus JS, Rapini RP, Shalita AR, et al, J Am Acad Dermatol. 1984;10(3):495–496</td>
<td>150</td>
<td>0.1mg/kg 0.5mg/kg 1.0mg/kg</td>
<td>20 weeks treatment 6- to 12-week follow up Patient questionnaire at 12- to 15 months</td>
<td>42% patients who received 0.1mg/kg/d required retreatment 20% patients who received 0.5mg/kg/d required retreatment 10% patients who received 1.0mg/kg/d required retreatment</td>
</tr>
<tr>
<td>Wakalek H, Hennew R, Schell, Vogt HJ. Retinoid Therapy: A Review of Clinical and Laboratory Research, Lancaster, England: MTP Press Limited, 1984:231–239</td>
<td>176</td>
<td>0.1mg/kg 0.5mg/kg 1.0mg/kg</td>
<td>12 weeks treatment 17-month follow up</td>
<td>First relapse in 0.1mg/kg/d group occurred 6 months after end of therapy All patients were in remission at 5 months 6 out of 26 patients had to restart acne treatment First relapse in 0.5mg/kg/d group occurred after 5 months First relapse in 0.1mg/kg/d group occurred after 2 months</td>
</tr>
<tr>
<td>Cunliffe WJ, Norris JFB, Dermatologica. 1987;179 (Suppl 1):133–137</td>
<td>250</td>
<td>0.5mg/kg 1.0mg/kg</td>
<td>4 months treatment 12- to 20-month follow up</td>
<td>Relapse rates: • 42% with 0.5mg/kg/d • 12% with 1mg/kg/d • P&lt;0.01</td>
</tr>
<tr>
<td>Layton AM, Knoops H, Taylor J, Cunliffe WJ, Br J Dermatol. 1993;129(3):292–296</td>
<td>88</td>
<td>0.5mg/kg 1.0mg/kg</td>
<td>16 weeks treatment 10-year follow up</td>
<td>39% relapsed and required oral antibiotics or further isotretinoin 82% patients who received &lt;120mg/kg cumulative dose relapsed vs. 30% who were given a larger dose (P&lt;0.01) Majority of patients relapsed within 3 years of isotretinoin therapy 78% patients relapsed within 18 months</td>
</tr>
<tr>
<td>Stainforth JM, Layton AM, Taylor JP, Cunliffe WJ, Br J Dermatol. 1993;129:297–301</td>
<td>299</td>
<td>0.1mg/kg 0.5mg/kg 1.0mg/kg</td>
<td>16 weeks treatment 5-year follow up</td>
<td>69% patients taking 0.1mg/kg/d isotretinoin who were followed relapsed 85% patients requiring more than 2 courses of isotretinoin were treated with 0.1mg/kg or 0.5mg/kg/d isotretinoin Only 9.5% patients needing ≥2 courses of isotretinoin were treated with 1mg/kg/d</td>
</tr>
<tr>
<td>White GM, Chen W, Yao J, Wee-Toastadis G, Arch Dermatol. 1998;134:376–378</td>
<td>179</td>
<td>Examined total cumulative dose</td>
<td>20 weeks treatment 3-year follow up</td>
<td>34.6% patients had no recurrence 46.5% patients receiving &gt;110mg/kg isotretinoin had no recurrence 40% patients receiving &gt;110mg/kg isotretinoin had no recurrence Chance of recurrence is 8.2 times for patients taking a total dose of &gt;100mg/kg vs. patients taking a total dose of ≤100mg/kg</td>
</tr>
<tr>
<td>Haryati I, Japinto SS, Int J Dermatol. 2005;44(12):999–1001</td>
<td>193</td>
<td>Examined total cumulative dose</td>
<td>10-year follow up</td>
<td>17.5% patients relapsed and were treated with topical therapy 3.3% patients relapsed and were treated with oral antibiotic plus topical therapy 19.6% patients relapsed and were treated with a second course of isotretinoin Total dose taken by patients who required further therapy was 103.5mg/kg for 6.7 months and 118.5mg/kg for 7.41 months for patients who were cured after one course</td>
</tr>
</tbody>
</table>

Review of studies evaluating oral isotretinoin dosing regimens, cumulative dosing, relapse rates, retreatment rates and acne therapies used.

**Lidose Oral Isotretinoin (Lidose-ISO) for Severe Recalcitrant Nodular Acne**

- **Open-label, Single-arm, Phase 4 Long-Term Study**
- **Active Treatment Phase (ATP)**
  - Administered for severe recalcitrant nodular acne
  - Ingested *WITHOUT FOOD*
  - Dosage: 0.5 mg/kg/day x 4 weeks then 1.0 mg/kg/day x 16 weeks
  - Total duration of therapy: 20 weeks
  - Attempted to approximate target cumulative dose of 120-150 mg/kg
- **Post-Treatment Phase (PTP)**
  - *2-year post-treatment follow-up* (weeks 32, 72, 98, 124)
  - Subjects stratified by Investigator Global Assessment (IGA) ratings
  - **Goal:** Assess Relapse Rates with use of LIDOS-ISO

Lidose Oral Isotretinoin (Lidose-ISO) Severe Nodular Acne (20 Weeks Treatment Without Food) Types and Rates of Retreatments Used Post-Treatment Period (Week 104)

Figure 4. Re-treatments Received in the PTP by Subgroup

Patients could be included in more than 1 re-treatment group if they had received more than 1 treatment type in the PTP. Subgroup of patients receiving prescription acne medication. OTC, over-the-counter; PTP, post-treatment period.

Lidose Oral Isotretinoin (Lidose-ISO) Severe Nodular Acne (20 Weeks Treatment Without Food) Types and Rates of Retreatments Correlated with Age Post-Treatment Period (Week 104)

Isotretinoin Mean Plasma Concentration
Micronized-Isotretinoin 32 mg vs Lidose-Isotretinoin 40mg
Time Curves in FASTED STATE

- Micronized-Isotretinoin TWICE as bioavailable as Lidose-Isotretinoin FASTED
  - SAME when FED
- Food: No effect on rate and marginal on extent of Micronized-Isotretinoin absorption
  - Less effect than on other marketed isotretinoin products

Standardized laboratory monitoring with use of isotretinoin in acne.

Hansen TJ 1, Lucking S 2, Miller AJ 3, Kirby JS 1, Thiboutot DM 1, Zeanglien AL 2.

Author information

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2 Pennsylvania State College of Medicine, Hershey, Pennsylvania.
3 Department of Dermatology, Pennsylvania State-Hershey Medical Center, Hershey, Pennsylvania; Department of Pediatrics, Pennsylvania State-Hershey Medical Center, Hershey, Pennsylvania. Electronic address: azaanglien@hmc.psu.edu.

Abstract

BACKGROUND: Laboratory monitoring for adverse effects to isotretinoin occurs with variability. Standardization of laboratory monitoring practices represents an opportunity to improve quality of care.

OBJECTIVE: We sought to develop an evidence-based approach to laboratory monitoring of patients receiving isotretinoin therapy for acne.

METHODS: We reviewed laboratory data from 515 patients with acne undergoing 574 courses of isotretinoin from March 2003 to July 2011. Frequency, timing, and severity of abnormalities were determined.

RESULTS: Clinically insignificant leukopenia or thrombocytopenia occurred in 1.4% and 0.9% of patients, respectively. Elevated liver transaminases were detected infrequently and not significantly increased compared with baseline detection rates (1.9% vs 1.6% at baseline). Significant elevations occurred with triglyceride (19.3%) and cholesterol (22.8%) levels. The most severe abnormalities were grade 2 (moderate). Mean duration of treatment before abnormalities were detected was 56.3 days for hypertriglyceridemia, 61.9 days for alanine transaminase, and 50.1 days for hypercholesterolemia.

LIMITATIONS: This was a single-center experience examining variable isotretinoin laboratory monitoring practices.

CONCLUSIONS: In healthy patients with normal baseline lipid panel and liver function test results, repeated studies should be performed after 2 months of isotretinoin therapy. If findings are normal, no further testing may be required. Routine complete blood cell count monitoring is not recommended.

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Serum Potassium Monitoring in Women Taking Oral Spironolactone for Acne

Low Usefulness of Potassium Monitoring Among Healthy Young Women Taking Spironolactone for Acne.

Pivankikh M1, Wang QY1, Mostaghimi A1

Abstract

IMPORTANCE: Spironolactone has been shown to be an effective treatment option for hormonally mediated acne but can cause hyperkalemia. The prevalence of hyperkalemia among healthy young women taking spironolactone for acne is unclear.

OBJECTIVE: To measure the rate of hyperkalemia in healthy young women taking spironolactone for acne or for an endocrine disorder with associated acne.

DESIGN, SETTING, AND PARTICIPANTS: Retrospective study of healthy young women taking spironolactone for acne. Data from December 1, 2000, through March 31, 2014, were obtained from a clinical data repository. Outpatient data were collected from 2 tertiary care centers in the United States. We analyzed rates of hyperkalemia in 974 healthy young women taking spironolactone for acne. We also analyzed 1165 healthy young women taking and not taking spironolactone to obtain a profile for the baseline rate of hyperkalemia in this population.

EXCLUSION CRITERIA: Cardiovascular disease, renal failure, and the use of medications that affect the renin-angiotensin-aldosterone system.

MAIN OUTCOMES AND MEASURES: The rate of hyperkalemia in healthy young women taking spironolactone for acne was calculated. Secondary measures included spironolactone prescribing profiles and potassium monitoring practices.

RESULTS: There were 10 abnormal serum potassium measurements in 1002 measurements obtained among young women receiving spironolactone therapy, yielding a hyperkalemia rate of 0.72%, equivalent to the 0.76% baseline rate of hyperkalemia in this population. Repeat testing in 6 of 13 patients demonstrated normal values, suggesting that these measurements may have been erroneous. In the remaining 7 patients, no action was taken.

CONCLUSIONS AND RELEVANCE: The rate of hyperkalemia in healthy young women taking spironolactone for acne is equivalent to the baseline rate of hyperkalemia in this population. Routine potassium monitoring is unnecessary for healthy women taking spironolactone for acne.

Avoid potassium sparing agents, potassium supplements, some anti-hypertensive agents (“PRILS”, “ARTANS”), caution in patients with renal impairment, lithium use.
THANK YOU

BACK IN 1971

WHAT THINGS COST
A first class stamp $0.06
A gallon of gas $0.36
A dozen eggs $0.53
A gallon of milk $1.18
A movie ticket $1.65

FEDERAL MINIMUM WAGE
$1.60
AN HOUR

'70s SLANG
Psyched! - Just kidding
Far Out! - Cool
Dream On - Unrestricted
Right On! - Agreement
Can You Dig It? - Do you understand?

IN THE NEWS...
The New York Times begins to publish sections of the Pentagon Papers, showing that the US Government had been lying to the American people.

Antrak is created to provide US inter city passenger train services.

Federal Express is started by Fred Smith.

The first soft contact lens became available commercially in the U.S.

The first Starbucks opens at the Pike Place Market in Seattle, Washington.

The Walt Disney World theme park opens in Florida.

IN THEATERS...
The Owl and the Pussycat
Summer of '42
Ryan's Daughter
The Aristocats
Love Story

ON TELEVISION...
All My Children
My Three Sons
McCloud
The Odd Couple
The Partridge Family

ON THE RADIO...
1. Joy to the World - Three Dog Night
2. Reason to Believe - Rod Stewart
3. I Feel the Earth Move - San Francisco
4. One Bad Apple - The Osmonds
5. How Can You Mend a Broken Heart - Bee Gees

USA:
U.S. PRESIDENT
Richard Nixon

TECHNOLOGY
Ray Tomlinson invented Internet email.

Intel releases world's first microprocessor, the 4004.

Texas Instruments releases the first pocket calculator.

Apollo 14 lands on the Moon.

The first internet chat rooms appear.

IN STYLE...
WOMEN
Polyester
Flared trousers
Platform shoes
Farrah Fawcett Flicks
MINI
V-neck velour shirts
Turtlenecks
Chest hair • Sideburns
Afros • Mullets