Resistance Concerns Steer Acne Tx From Antibiotics to Retinoids

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Prescribing has been gradually moving away from antimicrobial agents and toward increased use of retinoids in the treatment of acne vulgaris.

The shift toward nonantibiotics, reported in an analysis of national prescription habits between 1990 and 2002, may in part be explained by a growing awareness of antibiotic-resistant *Propionibacterium acnes,* wrote Dr. Suganthi Thevarajah and her associates in a poster presentation at the annual meeting of the American Academy of Dermatology.

The first report of antibiotic resistance to cutaneous *P. acnes* appeared in the late 1970s. The study showed that one in five U.S. patients treated with either topical erythromycin or clindamycin had resistant strains within their pilosebaceous follicles, noted Dr. Thevarajah of Hospital Kuala Lumpur, Malaysia. Dr. Thevarajah led the study while at the Center for Dermatology Research, Wake Forest University, Winston-Salem, N.C. The center is supported by a grant from Galderma Laboratories, which makes acne treatments.

She and her associates retrospectively analyzed data from all 4,922 acne visits from 1990 to 2002 in the National Ambulatory Medical Care Survey. The survey consists of outpatient information obtained from U.S. non–federally employed physicians.

During the 13-year period, there were significant declines in the likelihood of prescribing agents that relied on antimicrobial mechanisms for controlling acne. Included among these were benzoyl peroxide, topical clindamycin, oral erythromycin, and tetracycline-group antibiotics. In the same time period, there were significant increases in the likelihood of prescribing agents that were not dependent on antimicrobial mechanisms, such as topical retinoids and oral isotretinoin.

"Cross-resistance between erythromycin and clindamycin is increasing. This knowledge may have resulted in a decline in prescriptions for topical antibiotics as seen in our study," Dr. Thevarajah wrote.

Although the use of tetracycline-group antibiotics, including tetracycline, doxycycline and minocycline, decreased overall, their use actually increased among dermatologists. This may be because dermatologists are increasingly prescribing them for their anti-inflammatory effects rather than their antimicrobial properties, she added.

There was also a trend for dermatologists to have been more likely than nondermatologists to prescribe benzoyl peroxide, clindamycin, isotretinoin, topical retinoids, and tetracycline-group antibiotics.

Controls for demographic factors in the analysis did not change the findings about drug utilization.

A few demographic factors appeared to influence prescribing behavior. Older patients, for example, were less likely to receive clindamycin, topical retinoids, benzoyl peroxide, tetracycline-group antibiotics, and isotretinoin than younger patients. Men were less likely than women to receive clindamycin and topical retinoids and more likely to receive tetracycline-group antibiotics and oral isotretinoin. White patients were more likely to receive a prescription for isotretinoin but less apt to be given benzoyl peroxide, compared with nonwhite patients. ■

Combo Drug Duac Advantageous in Acne

BY BRUCE JANCIN
Denver Bureau

KOLOA, HAWAII — Duac, a clindamycin 1%/benzoyl peroxide 5% topical gel containing moisturizers and humectants, offers advantages for topical acne therapy, Dr. Leon H. Kircik said at the annual Hawaii dermatology seminar, which was sponsored by the Skin Disease Education Foundation.

The antibiotic and benzoyl peroxide combination acts synergistically on more of the underlying acne processes.

DR. KIRCIK

Amid growing concern about antibiotic resistance, long-term monotherapy with a topical antibiotic is difficult to justify, particularly when convincing evidence shows that adding benzoyl peroxide (BP) greatly reduces the resistance problem.

Moreover, the antibiotic/BP combination acts synergistically and addresses more of the underlying pathologic processes of acne than either agent alone, noted Dr. Kircik, a dermatologist in private practice in Louisville, Ky. "Neither topical erythromycin nor clindamycin alone has as much efficacy as benzoyl peroxide, so why use monotherapy unless the patient is allergic to benzoyl peroxide?" he asked.

BP's downside is that it's inherently drying, which impairs skin barrier function and reduces tolerability. Duac counteracts this by containing dimethicone as an occlusive agent to trap water in the skin as well as glycerin as a humectant to draw water to the stratum corneum from deeper layers.

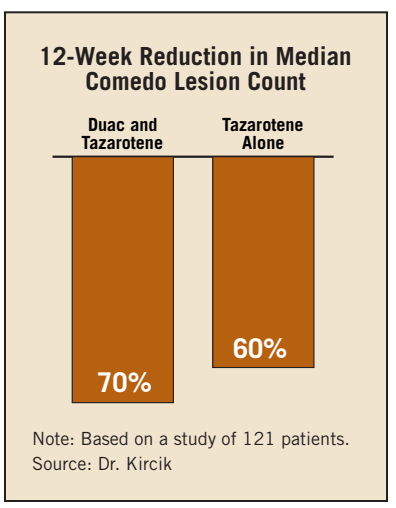
Dr. Kircik mentioned the results of a 12-week, double-blind, randomized clinical trial presented by Dr. Emil Tanghetti of the University of California, Davis, at last year's annual meeting of the American Academy of Dermatology in New Orleans. In that study, 121 adults with moderate to severe acne received Duac and tazarotene 0.1% cream once daily or tazarotene cream alone.

The median comedo lesion count dropped by 70% at 12 weeks in the combined treatment group, significantly better than the 60% decline in the retinoid monotherapy arm. Papules and pustules declined by 63% with combined treatment, compared with 58% with tazarotene alone. Most impressive of all, Dr. Kircik continued, was the significantly lower incidence of peeling in the combination therapy group at week 4.

Another study led by Dr. Tanghetti involved a head-to-head comparison of Duac and BenzaClin, a competing clindamycin 1%/BP 5% water-based gel that doesn't contain moisturizers. A total of 73% of the 52 participants in the evaluator-blinded, split-face, crossover study rated Duac as significantly better tolerated.

Dr. Kircik is a consultant to Stiefel Laboratories Inc., which markets Duac.

The SDEF and this news organization are wholly owned subsidiaries of Elsevier. ■



Data Don't Confirm Most Adverse Effects Of Isotretinoin

BY BRUCE JANCIN
Denver Bureau

KOLOA, HAWAII — Most of the reported adverse events associated with the use of isotretinoin for acne—aside from the oral retinoid's long-established teratogenicity risk—don't stand up to scrutiny, Dr. Lee T. Zane said at the annual Hawaii Dermatology Seminar sponsored by the Skin Disease Education Foundation.

Dr. Zane, a dermatologist at the University of California, San Francisco, provided details in the following areas regarding the reported adverse events:

▶ **Depression and suicidality.** Dr. Zane coauthored a recent systematic review of the literature that showed no support for a causal association between isotretinoin for acne and increased risk of depression or suicidal behavior.

But there's a catch: "The studies to date are either too small or otherwise limited enough that they can't rule out a weak association," according to Dr. Zane. "Until there is compelling evidence one way or the other, we absolutely must remain vigilant in our patient care in regards to psychiatric symptoms."

Dr. Zane's review included 214 published studies; most were case studies or low-quality research. Only nine reports included primary data—and only four of the nine used standardized depression rating scales. Of those four, none found any increase in depression scores during isotretinoin therapy, compared with pretreatment (Semin. Cutan. Med. Surg. 2005;24:92-102).

▶ **Hyperlipidemia and transaminases.** Dr. Zane is a coinvestigator in an ongoing retrospective cohort study of laboratory abnormalities in nearly 14,000 acne patients aged 13-50 in a large Northern California HMO. Fourteen percent had hypertriglyceridemia at baseline; this rate jumped to 50% during isotretinoin therapy. These real-world data were surprising; the Physicians' Desk Reference gives the hypertriglyceridemia rate in the isotretinoin clinical trials as 25%. The on-treatment incidence of triglyceride levels in excess of 1,500 mg/dL was 0.07% in the HMO study, with no values as high as 5,000 mg/dL.

Elevated transaminase levels were present in 5% of subjects prior to treatment and in 14% at some point during isotretinoin therapy, with 88% of on-treatment elevations being mild.

▶ **Acute pancreatitis.** There are only four published cases of what is believed to be isotretinoin-induced pancreatitis. All four involved overweight or obese women, two in their 40s. Two had triglyceride levels over 5,000 mg/dL at onset. One woman had a history of gallbladder disease. Another was on replacement estrogen, which is known to have a strong association with acute pancreatitis.

▶ **Benign intracranial hypertension.** In 179 reports of isotretinoin-associated benign intracranial hypertension, 24 reports involved prior or simultaneous use of tetracyclines. Mean time from isotretinoin exposure to diagnosis was 2.3 months. Symptoms cleared in 48% of patients upon stopping isotretinoin.

Based on the relatively quick onset of pseudotumor cerebri following isotretinoin exposure, the limited number of documented positive rechallenges, and the fact that hypervitaminosis A is a known cause, the investigators concluded that "it seems certain" that there is a direct correlation between isotretinoin use and benign intracranial hypertension (Ophthalmology 2004;111:1248-50).

Dr. Zane noted that neuro-ophthalmologic recommendations call for discontinuation of isotretinoin and a work-up for intracranial hypertension in patients who develop headache or unexplained blurred vision, along with avoidance of concomitant vitamin A, as well as tetracycline and other medications associated with benign intracranial hypertension.

The Skin Disease Education Foundation and this news organization are wholly owned subsidiaries of Elsevier. ■

Pages 38a—38b