Status Report From the American Acne & Rosacea Society on Medical Management of Acne in Adult Women, Part 2: Topical Therapies

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PRACTICE **POINTS**

- Data from randomized controlled clinical trials (RCTs) of topical agents used for the treatment of acne in adult women has been gleaned through subanalyses of larger pivotal studies with adapalene gel 0.3%, dapsone gel 5%, clindamycin phosphate 1.2%–benzoyl peroxide 3.75% gel, and adapalene 0.1%–benzoyl peroxide 2.5% gel.
- Efficacy and tolerability/safety results from RCTs of these topical agents evaluated outcomes for the clinical pattern of mixed inflammatory, comedonal, and non-nodular acne located on the face above the jawline margin.
- More data are needed on the treatment of acne in adult women with topical agents, systemic agents, and combination regimens, including results for the full spectrum of clinical presentations.

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This article is the second of a 3-part series. The third part will appear next month.
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In part 1 of this 3-part series, an overview of the epidemiology, visible patterns, and important considerations for clinical and laboratory evaluation of acne vulgaris (AV) in adult women was provided. Proper selection and integration of skin care products is important in the management of AV in this patient population. Part 2 of this series includes a discussion of over-the-counter and prescription topical therapies for adult women with AV. A summary of key randomized controlled trials also is provided. Further well-designed studies are needed, as data on the use of topical agents in this subpopulation are limited.

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It seems intuitive that clinicians in dermatology would automatically recognize the importance of proper selection and integration of skin care products and techniques in the management of acne vulgaris (AV). However, an understanding of the fundamental importance of skin care in AV management and the scientific basis for maintaining epidermal barrier (EpB) function and repair cannot be assumed. In fact, there is limited scientific information about EpB dysfunction and AV or the adjunctive benefits of specific skin care products. However, some data have emerged that can be successfully applied by clinicians.[1-9]

In part 2 of this series, emphasis is placed on skin care and topical therapies for the treatment of AV in adult women. In addition to the plethora of cleanser and moisturizer formulations that exist in the marketplace, there are many over-the-counter (OTC) products marketed to treat AV that contain benzoyl peroxide (BP) and salicylic acid. Importantly, women tend to be selective about what they use to cleanse and moisturize their skin, and use of OTC products to treat AV is common among adult women.[10,11]

A thorough discussion of EpB impairment, related inflammatory cascades, and potential relevance to AV are beyond the scope of this article. In short, appropriate skin care products can reduce the inflammation and sensitivity associated with increased transepidermal water loss and reduced stratum corneum hydration and can mitigate EpB impairments induced by certain acne medications or vehicles.[1,12] Available data support the adjunctive benefit of proper skin care in the management of AV by mitigating cutaneous irritation and potentially contributing to a reduction in AV lesions.[2-4,7,13] Use of a formulation that also provides broad-spectrum photoprotection also is helpful.[3,4]

Another challenge is the myriad of cosmeceuticals that are heavily marketed to adult women with AV.[13,14] Unfortunately, the scientific evidence supporting these products for treatment of AV is limited, resulting in the clinician's inability to make specific recommendations. The core message is to incorporate skin care products that can reduce EpB impairment and mitigate cutaneous irritation associated with some AV therapies.[1-4,7-9,12]

OTC Topical Therapies

The marketplace is replete with several OTC products for treatment of AV, most of which contain BP and salicylic acid.[15,16] There is a lack of efficacy data for OTC products for AV, including cleansers and topical medications, although some may be beneficial for milder cases. A variety of formulations are available to choose from, usually without the advice of a clinician. Additionally, heavy marketing is directed at adult women with AV, which may promote the use of therapies that may not be optimal for their respective AV severity or may cause facial skin irritation. Self-treatment may also cause delay in seeking dermatologic care, increasing the risk of persistent or permanent sequelae. Delay in adequate treatment is a major risk factor for the development of acne scars.[17]

Prescription Topical Therapies

Despite the high prevalence of AV in adult women, there is a paucity of studies evaluating topical therapies for AV in this subset.[18-24] Reports in the literature on AV in adult women have focused on systemic hormonal agents (eg, oral contraceptives, spironolactone); however, more recent reports have addressed the use of topical therapies in this subpopulation.[11,25-30] Published data on topical formulations are predominantly post hoc analyses from pivotal randomized controlled trials (RCTs) that included adolescents and adults of both genders with facial AV located above the jawline and predominantly moderate in severity.[11,26,28,30] Participants in all of these studies presented with non-nodular, mixed inflammatory, and comedonal facial AV above the jawline, with inclusion criteria that required a minimum of 20 comedonal lesions and 20 papulopustular lesions at baseline. An important differentiating factor among these various post hoc analyses evaluating adult women versus adolescent girls with AV are the ages used to separate adults from adolescents. A dividing line of 18 years and older was used in some reports (eg, adapalene gel 0.3%, dapsone gel 5%), while other reports used 25 years and older to separate adolescent girls from adult women (ie, clindamycin phosphate [CP] 1.2%–BP 3.75% gel, adapalene 0.1%–BP 2.5% gel).[11,26,28,30]

Importantly, these studies included adult women with AV who presented with mixed comedonal and inflammatory AV (mixed pattern AV) similar to adolescents. None of the studies included women with a *U*-shaped AV pattern or lower facial AV characterized by deep inflammatory lesions that are often tender and few in number. Unfortunately, there is a lack of data evaluating topical therapies for these patterns of AV in adult women, including AV below the jawline and on the trunk. Although mixed pattern AV has been reported to affect 75% to 90% of adult women with AV, epidemiologic data quantifying the clinical AV patterns affecting adult women are limited.[11,22,29,31,32] More well-designed studies are needed.

The treatment of AV in adult women may incorporate any of the topical therapies used to treat AV in adolescents, especially as studies encompass both the adolescent and adult age ranges. This is especially true with mixed pattern AV, which is the predominant presentation in participants enrolled in clinical trials with topical therapies, especially of moderate severity.

Herein we provide a summary of the topical therapies that have been evaluated by post hoc analyses of data from pivotal studies in adult women with AV.

Adapalene Gel 0.3%—Adapalene exhibits retinoid activity with efficacy in reducing inflammatory and comedonal AV lesions shown with both 0.1% and 0.3% concentrations.[33-35] Post hoc analyses of 2 pivotal RCTs of patients with facial AV showed that adapalene gel 0.3% once daily (n=74; mean age, 27.2 years) was superior to vehicle once daily (n=43; mean age, 25.2 years) in both mean and median percentage reductions of comedonal, inflammatory, and total lesions in women 18 years and older who were treated for 12 weeks; the difference in mean percentage lesion reduction from vehicle for total AV lesions was statistically significant at 12 weeks (P=.045).[26] Adapalene gel 0.3% produced a favorable skin tolerability profile similar to adapalene gel 0.1%, with the most common adverse reactions being discomfort and dryness.

Advantages of topical retinoid therapy in adult women with facial AV are reduction in postinflammatory hyperpigmentation and therapeutic modulation of chronic photodamage (eg, fine lines, rough texture, dyschromia).[29,36,37] Disadvantages include signs and symptoms of cutaneous irritation, although this tends to occur less frequently on facial skin with adapalene gel 0.3% as compared to other topical retinoids that exhibit comparable efficacy.[33-37] Topical retinoid therapy on the anterior neck and upper chest should be used cautiously, as these anatomic sites appear to be more prone to cutaneous irritation.

Dapsone Gel 5%—Dapsone is a sulfone antimicrobial and anti-inflammatory agent that has been shown to be effective, safe, and well tolerated in the treatment of AV in a topical 5% formulation.[38,39] A post hoc analysis of pivotal 12-week trial data suggested that dapsone gel 5% twice daily produced greater AV reductions in females compared to males; no gender differences were noted in adverse effects, which were low in frequency.[39] A separate subgroup analysis compared outcomes among adult women (≥18 years of age; n=434) and adolescent girls (12–17 years of age; n=347) treated with dapsone gel 5%.[11] The proportion with no or minimal acne based on the Global Acne Assessment Score at week 12 was greater in adult women (53.5%) versus adolescent girls (45.3%, P=.022), with significantly greater percentage reductions in both noninflammatory (P<.0001) and total lesion counts (P=.0008) observed in the adult group. Percentage reductions in inflammatory lesions were similar in both groups. No major safety or tolerability issues or new safety signals were noted. Advantages of dapsone gel 5% are highly favorable tolerability and the perception of decreased oily skin in some participants.[38,39]

Clindamycin Phosphate 1.2%–Benzoyl Peroxide 3.75% Gel—The combination formulation of CP 1.2%–BP 3.75% gel applied once daily has been shown to be effective, well tolerated, and safe for the treatment of facial AV, with a gender analysis noting an apparent greater efficacy in females.[40,41] A post hoc analysis from the 12-week pivotal study data in adult women aged 25 years and older showed a mean percentage change from baseline in inflammatory and noninflammatory lesion counts and the percentage of participants who achieved a 2-grade improvement by global assessment to be 68.7%, 60.4%, and 52.7% in actively treated participants (n=29), respectively, which was significantly superior to vehicle applied once daily (n=43; P=.019, P=.020, and P=.074, respectively).[42] No relevant differences in tolerability were noted among treatment groups, and no participants discontinued therapy due to adverse events. Advantages of CP 1.2%–BP 3.75% gel are highly favorable skin tolerability and the perception of decreased oily skin in some participants.[41-43]

Adapalene 0.1%–Benzoyl Peroxide 2.5% Gel—A meta-analysis of pooled data from 3 RCTs evaluated use of adapalene 0.1%–BP 2.5% gel applied once daily in adult women aged 25 years and older with facial AV (n=130) versus vehicle gel applied once daily (n=124).[30] The percentage of participants who achieved investigator global assessment ratings of clear or almost clear was 39.2% in actively treated participants versus 18.5% with vehicle (P<.001), and median percentage lesion reduction

was approximately 30% greater in those treated with adapalene 0.1%–BP 2.5% gel versus vehicle gel. Tolerability and safety were favorable.

Other Agents—Topical azelaic acid (20% cream formulation, 15% gel formulation) has been suggested as a treatment option for adult women with AV, including patients with darker skin who are more prone to persistent hyperpigmentation.[29]

Conclusion

Proper skin care is an important component in the management of AV in adult women. Data for topical therapies in this subpopulation are limited; however, post hoc analyses provide some information regarding their efficacy in treating mixed pattern AV. More well-designed studies are needed to better evaluate the use of topical agents in adult women with AV. Although most topical AV therapies appear to be safe for use during pregnancy when properly used and limited to facial application, their use in women of childbearing potential and during pregnancy warrants individual consideration; topical retinoids are best avoided during pregnancy, especially tazarotene, which is rated category X.[44] In part 3 of this series, oral therapies used to treat AV in adult women will be discussed.

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