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Review Article

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The Rational of a Fixed Combination of Benzoyl Peroxide and Niacinamide in the Treatment of Acne Vulgaris: A Narrative Review

Massimo Milani* and Francesca Colombo

Cantabria Labs Difa Cooper Medical Department, Caronno Pertusella (VA), Via Milano 160; Italy

***Corresponding Author**
Massimo Milani, Cantabria Labs Difa Cooper Medical Department, Caronno Pertusella (VA), Via Milano 160; Italy.

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Abstract

Acne vulgaris (AV) in a common skin disease affecting mainly adolescents but could be present also in adult subjects. AV is characterized by the presence of non-inflammatory (comedons) and inflammatory (papules, pustules, cysts, and nodules) lesions affecting sebaceous glands rich regions like the face, back, shoulder and thorax. A central pathogenetic role of AV lesions seems played by Cutibacterium acnes, especially some phylotypes (i.e. C. acne IA1) able to induce an inflammatory response at the level of sebaceous glands. Other important pathogenetic factors of AV are the androgen-driven increase of sebum production and the process of hyperkeratinisation of the infundibulum. The first line treatment of AV is in general done using monotherapy with antibacterial agents like benzoyl peroxide (BPO) and hydrogen peroxide or topical retinoid molecules. These two classes of drugs could interfere with C. acnes growth (BPO) and with keratinocytes proliferation (retinoid). Fixed combination of BPO and retinoid molecules are commonly used in mild to moderate forms of AV. However, both BPO and retinoids could be nor well tolerated especially during the first weeks of treatment causing skin irritation erythema and dryness. Both BPO and topical retinoids could interfere with the skin barrier function. During BPO treatment the Trans epidermal water loss (TEWL) a marker of skin barrier function, increase significantly supporting the fact that BPO alters this function. Niacinamide is a potent anti-inflammatory molecule able to preserve the skin barrier function. Niacinamide has shown to be effective in AV with inflammatory lesions. There is a strong rationale for the development of a topical product formed by fixed combination of BPO and niacinamide for the first-line treatment of mild to moderate AV but also in the treatment of papulopustular rosacea. In this narrative review we discuss the rational of the combination and the first clinical data of this product as first line AV and rosacea treatment strategy.

Keywords: Acne, Rosacea, Benzoyl Peroxide, Niacinamide, Fixed Combination.

1.Introduction Acne Vulgaris and Rosacea Pathogenesis and the Rational of Treatment

Acne vulgaris (AV) is a common skin inflammatory disease affecting the pilosebaceous unit [1]. AV pathogenesis involves four main processes: increase in sebum production; follicular hyperkeratinisation with sebaceous follicles obstruction; *Propionibacterium acnes (Cutibacterium acnes)* proliferation; and inflammation [2]. Some strains of C. acnes (IA1) are crucial in starting the inflammatory response in the AV lesions formation [3]. Colonisation of the pilosebaceous follicle by C. acnes is considered as a main factor causing acne by inducing the inflammatory response of the skin [4]. Two other factors playing a relevant role in this chronic inflammatory skin disease are the quantitative and qualitative modification of sebum production, with a modification of its composition, and the hyper cornification process of the pilosebaceous follicle resulting from hyperproliferation and abnormal differentiation of keratinocytes [5]. Environmental factors, hormones, family history and stress are also other contributing factors that influence the severity as well the incidence and persistence of acne [6]. AV is characterized by an alteration in the skin barrier function even in absence of anti-acne aggressive treatments such as oral or topical retinoids [7]. Rosacea is a very common, chronic inflammatory disease characterized by flushing, erythema, and inflammatory lesions, affecting the face [8]. Inflammatory lesions of Rosacea (papules and pustules) are very similar to the AV inflammatory lesions even if the are characterized by some difference in the distribution in the regions of the face [9]. Also, rosacea is characterized by a relevant skin barrier function alteration [10]. Commonly, AV is treated using topical products, alone or in combination, such as benzoyl peroxide (BPO), retinoids and antibiotics [11]. These classes of drugs could interfere with *C. acnes* growth (BPO and antibiotics) and with keratinocytes proliferation (retinoid). Fixed combination of BPO and retinoid molecules are commonly used in mild to moderate forms of AV [12]. However, both BPO and retinoids could be not well tolerated especially during the first weeks of treatment causing skin irritation erythema and dryness with negative influences on the compliance to the treatment [13]. Clinical success of acne treatments is deeply influenced by adherence or compliance to the therapy [14]. Low skin

tolerability and/or low efficacy are the main reason of the lack of compliance. Therefore, an ideal treatment for AV could be able to interfere with the pathogenetic mechanisms involved in AV lesions formation. Topical metronidazole or topical and oral antibiotics like doxycycline are used in the treatment of inflammatory Rosacea [15]. BPO is not commonly used in Rosacea due to its irritative action on the skin, even if new formulation of BPO have recently showed to be effective and well tolerated also in this skin condition [16].

2. Benzoyl Peroxide and Niacinamide: Drugs Characteristics

Benzoyl peroxide (BPO) and niacinamide (Niac) are commonly used alone or in combination with other molecules in the treatment of acne [17]. Niac is also commonly used alone or in combination with other molecules in Rosacea treatment [18]. Topical niacinamide can provide appearance benefits in rosacea patients by improving skin barrier properties [19]. BPO is a very effective topical product able to express bacteriostatic but also bactericidal activity against C. acnes trough its powerful oxidizing activity BPO has also keratolytic effects [20]. Topical BPO is indicated for the treatment of mild-to-moderate acne vulgaris. However, BPO can have, especially during the initial treatment phases a low skin tolerability with skin erythema and a negative effect of skin barrier function [21]. During treatment with BPO the Trans Epidermal water loss can increase up to 80%, demonstrating that BPO can alter skin barrier function [22]. Niacinamide, an amide of vitamin B3 (niacin), is a hydrophilic endogenous substance. Its effects after topical application have been described in the scientific literature. Niacinamide has antipruritic, antimicrobial, vasoactive, photo-protective, sebostatic and lightening effects depending on its concentration [23]. Niacinamide is a well-tolerated and safe substance often used in cosmetics. Clinical data for its therapeutic use in various dermatoses can increasingly be found in the literature. Although the existing data are not sufficient for a scientifically founded evaluation, it can be stated that the use of niacinamide in galenic preparations for topical application offers interesting prospects. Niac is able also to increase levels of ceramides and free fatty acids in the epidermis and decreases the trans-epidermal water loss (TEWL), so facilitating epidermal cells to improve the epidermal permeability barrier and moisturization degree [24]. Several reviews support the use of Niac is effective in acne and rosacea.

3. Fixed Combination of Benzoyl peroxide and Niacinamide

Fixed combinations of BPO and Niac have been recently developed and commercialized as cosmeceutics or medical device products. Combing BPO and Niac in the same product could have the advantage to express complementary and synergistic effects improving efficacy and skin tolerability in acne but also in rosacea. Furthermore, Niac could reduce some side effects of BPO, such as skin irritation and erythema and counteracting the negative effect of BPO on the TEWL. The table summarizes the rational of the combination in comparison with the single components.

	BPO alone	Niac alone	BPO+Niac.
Antibacterial action	++	+	+++
Sebum production reduction	+	+	++
Keratolytic and comedolytic activities	++	-	++
Anti-inflammatory activity	-	++	++
Possibility to be used in inflammatory AV	++	-	+++
Possibility to be used in inflammatory Rosacea	No	Yes	Yes
Skin barrier alteration	yes	no	no

Table: Rational of the Fixed Combination of Benzoyl peroxide and Niacinamide in acne and Rosacea in comparison with single components

Unpublished data (Puviani et al personal communication) suggest that this combination is very effective as monotherapy treatment of mild-to moderate AV without affecting TEWL. Preliminary data suggest also that this product is well tolerated in rosacea patients. Interesting, the use of this fixed combination has reduced non-inflammatory and inflammatory acne lesions by 43% in comparison with baseline, without affecting TEWL values. This fixed combination is able to reduce sebum production by 42% in comparison with pre-treatment values. Future controlled clinical studies are warranted to better define the efficacy and safety profile of this new therapeutic strategy.

4. Conclusion

The treatment of Acne vulgaris and Rosacea is commonly done using topical products alone or in combination. Both Acne Vulgaris and Rosacea are clinical condition characterized by skin barrier function alteration. Therefore, skin tolerability of the acne and rosacea treatments is a relevant factor in order to improve compliance to the therapy. A fixed combination of BPO and Niac is a very promising therapeutic approach for both these skin conditions. Preliminary data seem to suggest that this combination could have synergistic and complementary actions optimizing efficacy and skin tolerability and barrier function. Future clinical controlled data could confirm these preliminary observations.

References

1. Williams, H. C., Dellavalle, R. P., & Garner, S. (2012). Acne vulgaris. *The Lancet, 379*(9813), 361-372.
2. Zaenglein, A. L. (2018). Acne vulgaris. *New England Journal of Medicine,* 379(14), 1343-1352.
3. Dréno, B., Pécastaings, S., Corvec, S., Veraldi, S., Khammari, A., & Roques, C. (2018). Cutibacterium acnes (Propionibacterium acnes) and acne vulgaris: a brief look

at the latest updates. *Journal of the European Academy of Dermatology and Venereology,* 32, 5-14.
4. Beylot, C., Auffret, N., Poli, F., Claudel, J. P., Leccia, M. T., Del Giudice, P., & Dreno, B. (2014). Propionibacterium acnes: an update on its role in the pathogenesis of acne. *Journal of the European Academy of Dermatology and Venereology,* 28(3), 271-278.
5. Li, X., He, C., Chen, Z., Zhou, C., Gan, Y., & Jia, Y. (2017). A review of the role of sebum in the mechanism of acne pathogenesis. *Journal of cosmetic dermatology,* 16(2), 168-173.
6. Ju, Q., Zouboulis, C. C., & Xia, L. (2009). Environmental pollution and acne-chloracne. *Dermato-endocrinology,* 1(3), 125-128.
7. Thiboutot, D., & Del Rosso, J. Q. (2013). Acne vulgaris and the epidermal barrier: is acne vulgaris associated with inherent epidermal abnormalities that cause impairment of barrier functions? Do any topical acne therapies alter the structural and/or functional integrity of the epidermal barrier?. *The Journal of clinical and aesthetic dermatology,* 6(2), 18.
8. Powell, F. C. (2005). Rosacea. *New England Journal of Medicine,* 352(8), 793-803.
9. van Zuuren, E. J. (2017). Rosacea. *New England Journal of Medicine,* 377(18), 1754-1764.
10. Culp, B., & Scheinfeld, N. (2009). Rosacea: a review. *Pharmacy and Therapeutics,* 34(1), 38.
11. Thiboutot, D., Gollnick, H., Bettoli, V., Dréno, B., Kang, S., Leyden, J. J., ... & Wolf Jr, J. (2009). New insights into the management of acne: an update from the Global Alliance to Improve Outcomes in Acne group. *Journal of the American Academy of Dermatology,* 60(5), S1-S50.
12. Musumeci, M. L., Schlecht, K., West, D. P., West, L. E., Innocenzi, D., & Micali, G. (2005). Topical treatment of acne vulgaris: A review. *Giornale Italiano di Dermatologia e Venereologia,* 140(6), 713-722.
13. Fares, H. M., Chatterjee, S., & Hayward, M. (1996). In vitro permeation and irritation of benzoyl peroxide-containing products. *International journal of pharmaceutics,* 133(1-2), 215-222.
14. de Lucas, R., Moreno-Arias, G., Perez-López, M., Vera-Casaño, Á., Aladren, S., Milani, M., & ACTUO Investigators study group. (2015). Adherence to drug treatments and adjuvant barrier repair therapies are key factors for clinical improvement in mild to moderate acne: the ACTUO observational prospective multicenter cohort trial in 643 patients. *BMC dermatology,* 15, 1-6.
15. Two, A. M., Wu, W., Gallo, R. L., & Hata, T. R. (2015). Rosacea: part II. Topical and systemic therapies in the treatment of rosacea. *Journal of the American Academy of Dermatology,* 72(5), 761-770.
16. Breneman, D., Savin, R., VandePol, C., Vamvakias, G., Levy, S., & Leyden, J. (2004). Double-blind, randomized, vehicle-controlled clinical trial of once-daily benzoyl peroxide/clindamycin topical gel in the treatment of patients with moderate to severe rosacea. *International journal of dermatology*, 43(5), 381-387.
17. Farrisa, M. T. P. (2021). Cosmeceuticals for Acne and Rosacea. *Cosmeceuticals*, 82.
18. Geng, R., Bourkas, A. N., & Sibbald, R. G. (2023). Rosacea: Clinical Aspects and Treatments. *Advances in Skin & Wound Care*, 36(12), 626-634.
19. Draelos, Z. D., Ertel, K., & Berge, C. (2005). Niacinamide-containing facial moisturizer improves skin barrier and benefits subjects with rosacea. *CUTIS-NEW YORK-*, 76(2), 135.
20. Valacchi, G., Rimbach, G., Saliou, C., Weber, S. U., & Packer, L. (2001). Effect of benzoyl peroxide on antioxidant status, NF-κB activity and interleukin-1α gene expression in human keratinocytes. *Toxicology*, 165(2-3), 225-234.
21. Weber, S. U., Thiele, J. J., Han, N., Luu, C., Valacchi, G., Weber, S., & Packer, L. (2003). Topical α-tocotrienol supplementation inhibits lipid peroxidation but fails to mitigate increased transepidermal water loss after benzoyl peroxide treatment of human skin. *Free Radical Biology and Medicine*, 34(2), 170-176.
22. Milani, M. (2013). Acne, anti-acne therapies and epidermal barrier functions: the role of adjuvant treatments. *OA Dermatology,* 1(1), 4.
23. Matts, P. J., Oblong, J. E., & Bissett, D. L. (2002). A review of the range of effects of niacinamide in human skin. *Int Fed Soc Cosmet Chem Mag,* 5(4), 285-289.
24. Rolfe, H. M. (2014). A review of nicotinamide: treatment of skin diseases and potential side effects. *Journal of cosmetic dermatology,* 13(4), 324-328.