Rebalancing of the skin microbiome with an emollient 'plus' for effective management of atopic dermatitis: A mini review

Chin Chwen Ch'ng, MRCP, AdvMDerm

Subang Jaya Medical Centre, Subang Jaya, Selangor, Malaysia

ABSTRACT

A balanced and diverse skin microbiome is pivotal for healthy skin. Dysregulation of the skin microbiome could disrupt the skin barrier function and result in the development of atopic dermatitis (AD), a common chronic and relapsing inflammatory skin disorder. Given the role that the skin microbiome plays in the initiation and maintenance of AD, maintaining a healthy skin microbiome is crucial for effective disease management. Specifically, current guidelines recommend emollients as the treatment mainstay in maintaining a functional skin barrier across disease severity. Emollient 'plus' or therapeutic moisturisers have recently emerged as the next-generation emollients that specifically aim to rebalance the skin microbiome and subsequently improve AD lesions. This article provides a quick overview of an emollient 'plus' or therapeutic moisturiser, discussing the clinical efficacy and tolerability of Lipikar Baume AP+M as a companion in AD management.

KEYWORDS:
Skin microbiome, barrier function, atopic dermatitis, emollient 'plus', therapeutic moisturiser

INTRODUCTION

Human skin is colonised by an abundant and diverse population of microorganisms, called microbiome, that coexist with human skin cells in an intricately controlled environment.[1] These microbial communities support the overall skin health through their interaction with the host, such as by reinforcing the physical and immunological barriers of the skin.[1] The skin uses several mechanisms to control its microbiome, including regulation of pH, water content, lipid composition and antimicrobial peptides (AMPs).[1]

Dysregulation in any of these systems could cause an imbalance in the skin microbiome, represented by an overabundance of one microbial species or a decrease in overall microbial diversity, a condition known as 'dysbiosis'.[1] In many instances, dysbiosis could disrupt skin homeostasis and lead to the development of many chronic skin diseases, including atopic dermatitis (AD).[1]

AD is a chronic relapsing and remitting inflammatory skin disorder characterised by dry skin, localised erythema, pruritus and skin pain. AD is a common condition that affects up to 10% of adults and up to 20% of children worldwide.[2] AD exacts a substantial burden on patients and their families through its effect on health-related quality of life (HRQoL) and socioeconomic costs,[3] making it an important public health problem worldwide.

Skin Microbial Dysbiosis and AD

Dysbiosis is well documented in patients with AD, with evidence showing heavy colonisation of *Staphylococcus aureus* and loss of microbial diversity in AD skin compared with the skin of healthy individuals.[4] Specifically, *S. aureus* is associated with and often preceded AD flares,[5] and the degree of *S. aureus* colonisation correlates with disease severity.[5]

S. aureus initiates and exacerbates AD by exploiting mechanisms that affect the skin barrier function and skin immunity.[1,6] In a nutshell, *S. aureus* colonisation on the skin can lead to biofilm production, causing disruption in the skin barrier function and permitting entry of infectious agents into the dermis, resulting in chronic inflammation and skin immunity impairment.[1,6] Therefore, maintaining a balanced and diverse microbial population is crucial for overall cutaneous health.

Current Guidelines for AD Management

International,[7] regional[8] and local[9] guidelines recommend a stepped-care approach for AD management, involving regular use of emollients and additional therapies based on disease severity. As the quantity of emollients is essential for effective AD control, the European guidelines recommend prescribing a minimum amount of 250 g per week for adults.[7] Meanwhile, the Asian guidelines recommend prescribing 120 to 225 g per week for adults and 40 to 75 g per week for children aged 4 years.[8]

While current guidelines do not offer specific recommendations on targeted support to improve the skin microbiome as an initial treatment approach, various AD therapies have been shown to reduce the abundance of *S. aureus* and improve microbial diversity, leading to effective disease control. Accordingly, the Malaysian guidelines and others recommend identifying and managing aggravating factors, such as microbial colonisation, for better AD control.[9] More specifically, the European guidelines have now recognised the role of emollient 'plus' or therapeutic moisturisers in improving AD lesions and regulating skin microbiome in patients with AD.[7]

Skin Microbiome Rebalancing with an Emollient 'Plus': Evidence of Clinical Efficacy and Tolerability

Lipikar Baume AP+M (La Roche-Posay Laboratoire Dermatologique, France) is an emollient 'plus' specifically formulated for AD skin. Multiple studies of patients with

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Corresponding Author: Chin Chwen Ch'ng
Email: chinchwen@gmail.com

mild-to-moderate AD demonstrated that Lipikar Baume AP+M has higher efficacy in modulating the skin microbiome compared with commercial emollients.[10,11] In particular, patients receiving Lipikar Baume AP+M had a higher reduction of the *S. aureus* population and a significant increase in the *Xanthomonas* genus than those receiving the usual emollient, despite using less product.[10]

Compared with the usual emollient, Lipikar Baume AP+M monotherapy led to significant improvement in the average Scoring Atopic Dermatitis (SCORAD) level, corresponding with an 11% reduction in SCORAD level at Day 28 ($p = 0.018$).[10] A recent longer-term follow-up study showed that Lipikar Baume AP+M monotherapy significantly improved the SCOARD, signs and symptoms at Day 168 versus the baseline period in patients with mild-to-moderate AD (all $p < 0.05$).[12] Notably, patients receiving Lipikar Baume AP+M were twice less likely to experience relapse within 28 days of follow-up than with usual emollients.[10] Lipikar Baume AP+M also reduced the number and intensity of flares in the longer-term follow-up study.[12]

A significant steroid-sparing effect was also observed with Lipikar Baume AP+M without affecting its efficacy.[13] In patients with mild-to-moderate AD receiving topical corticosteroids (TCS), the addition of Lipikar Baume AP+M significantly reduced TCS use by 34% compared with a routine emollient ($p = 0.041$), driven by the decrease in the number of TCS applications per days and the number of days of TCS use.[13] When used as an adjunct to systemic agents, Lipikar Baume AP+M led to a significantly greater reduction in current pruritus of moderate-to-severe AD at Week 10 ($p = 0.0277$), even with less product use.[14] In addition, the improvement in patient global assessment and SCORAD scores were greater with Lipikar Baume AP+M versus the usual emollient.[14]

Importantly, daily use of Lipikar Baume AP+M monotherapy for 6 months resulted in a significant improvement in the HRQoL of patients with mild-to-moderate AD over time ($p <0.001$).[12] Similarly, patients with moderate-to-severe AD receiving adjunct Lipikar Baume AP+M had a 20% reduction in the Dermatology Life Quality Index (DLQI) score than the control group, with patients receiving Lipikar Baume AP+M reporting significantly better responses for DLQI items #6 and #7.[14] The studies showed that Lipikar Baume AP+M as monotherapy or adjunct therapy has a good safety profile,[12,14] with high overall tolerance and satisfaction rate of over 96%.[15]

Notably, two cost-effectiveness analyses conducted in the UK (including lost productivity cost)16 and France (only direct healthcare costs)17 showed that Lipikar Baume AP+M was the more cost-effective strategy for relapse prevention than other commercially tested emollients and no emollients. Compared with emollients of a similar price range, patients using Lipikar Baume AP+M will have an additional 1.08 to 4.92 months without flares over 6 years of follow-up.[17] Similarly, Lipikar Baume AP+M will generate a respective gain of 1.08, 3.84 and 6.12 months without flares compared with less costly, more costly and no emollients over 6 years.[17]

The microbiome maintenance action of Lipikar Baume AP+M is thought to be driven by the active ingredients *Vitreoscilla filiformis* and microresyl.[18] The *V. filiformis* biomass extract has been shown to activate endogenous cutaneous antioxidants and increase the secretion of AMPs via the toll-like receptor 2 and protein kinase C signalling pathway to effectively control inflammation in AD.[18] Extracted from Ophiopogon japonicum tuberous roots, microresyl has been shown to reduce the inflammatory markers on the skin cells (such as thymic stromal lymphopoietin and interleukin 8) and limit *S. aureus* adhesion to the skin.[19]

Another emollient 'plus', Dermoflan AD cream (Meda Pharma, Sweden), has also been shown to exhibit microbiome maintenance properties, attributed to the selective antibacterial and prebiotic activities of galacto-oligosaccharides and xylitol.[20] Dermoflan AD cream significantly increased microbial diversity in treated areas at Day 28 versus baseline among participants predisposed to AD.[20] The author concluded that larger studies are needed to study the correlation between changes in the skin microbiome after Dermoflan AD cream treatment and clinical improvement of AD.[20]

CONCLUSION

Skin microbiome dysbiosis is a key component of atopic dermatitis (AD) disease initiation and progression. Therapies that aim to rebalance the skin microbiome can reduce S. aureus abundance, increase microbial diversity in AD skin could help maintain a functional skin barrier and improve disease management. By rebalancing the skin microbiome, Lipikar Baume AP+M has been shown to be effective as monotherapy or adjunct therapy in AD management, representing the most cost-effective strategy in AD relapse prevention.

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