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Review article

Skin Challenges in Covid-19 Pandemic: The Importance of Cosmeceuticals

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SUMMARY

Introduction. Although COVID-19 is present in a milder form nowadays, systemic disorders caused by the virus lead to multiple organ malfunctions. Skin manifestations are the consequence of the disease itself but also the result of preventative measures taken to avoid the infection. They generally do not require pharmacotherapy except in severe cases. Depending on severity of COVID-19-related skin disorder, cosmeceuticals are often recommended in their management. In this study, we highlighted skin adverse events related to all aspects of COVID-19 pandemic aiming to provide a comprehensive overview and enlighten the role of cosmeceuticals in the treatment of those skin issues, according to published studies and guidelines.

Methods. Different steps were conducted in preparation of this review- identification of all factors that affect skin in pandemics (protective measures, disease itself, post-COVID syndrome), selection and classification of reported skin symptoms which could be managed using cosmeceuticals, according to relevant papers and guidelines.

Discussion. Skin challenges in COVID-19 pandemics could be divided into three main categories: 1) Cutaneous manifestations of COVID-19 disease; 2) Cutaneous symptoms as a result of wearing protective equipment and using disinfectants, and 3) Cutaneous symptoms related to the post COVID-19 syndrome.

Conclusion. Cosmeceuticals, a unique category of products between cosmetics and pharmaceuticals, are highly recommended in literature for the management of aforesaid changes except in severe skin disorders. Since the introduction of cosmeceutical concept, those topicals have become an extremely important part of dermatologist's armamentarium. COVID-19 pandemic confirms their importance.

Keywords: **cosmeceuticals, COVID-19, pandemic, post-COVID, skin**

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus, in its hardest form, is followed by severe pneumonia, acute respiratory distress syndrome, septic shock and multiple organ failure. However, COVID-19 is present in a mild form much more often, affecting many organs including the skin, dysregulating many areas of metabolism including skin lipidome (1, 2).

Now, four years after the beginning of pandemic, it is obvious that COVID-19 has high-lighted different areas of skin damage. Some of them have previously been described in literature, but not necessarily as mainstream topics. For example, ''maskne'' (term coined during pandemic), skin disorder usually well-recognized in some groups of healthcare workers, became very common in general population and associated with personal protective equipment (PPE) (3). Frequent use of hygiene measures such as sanitizer gels, hand washing etc. is usually associated with compromised skin barrier function. With the beginning of pandemic, those measures became mandatory, and their use increased the frequency of associated skin disorders which are usually described as mild. In the management of both facial and hand skin issues, different cosmeceuticals have been recommended (4).

However, this is not the end of the list of COVID-19 skin issues.

Recently, WHO introduced the term "long COVID" (or post COVID) syndrome as the lack of patient's ability to recover from different symptoms associated with COVID-19 even after months from the peak of the disease. Fatigue, shortness of breath, cognitive dysfunction etc. generally have an impact on everyday functioning. Different cutaneous "long COVID" symptoms were also reported (5, 6).

In summary, skin manifestations in COVID-19 are numerous and could be a consequence of the disease itself, but also of the preventative measures taken to avoid the infection (7). The consequences of constant hand washing and sanitizer use, mask wearing, psychological stress, "long illness" pushed consumers to protect and take care of their skin harder than before. Public health crisis confirmed a major trend in the skincare category: consumers are increasingly interested in skin health and safe, effective cosmeceuticals recommended by health care professionals. Cosmeceuticals, or dermocosmetics represent a borderline class of topical products between pharmaceutical preparations and skin care products. However, there is still no precise definition and legal framework for classification of cosmeceuticals. They are generally seen as "active" cosmetic products that achieve physiologically relevant benefits on the skin (in terms of "anti-aging", antioxidant, exfoliating and other effects), although they do not contain active pharmaceutical ingredient, i.e. they do not belong to the class of drugs. Currently, dermocosmetic products are the subject to legal regulations for cosmetic products although they cannot be equated with "classic" cosmetics.

Herein, we have striven to summarize the skin adverse events related to all aspects of COVID 19 pandemic and to provide a comprehensive overview of cosmeceuticals which could be used in the treatment of those skin conditions, according to published studies and guidelines. We aimed to emphasize that the skin, as the primary protective and most superficial human organ, is affected with pandemic in many different ways, and carefully selected cosmeceuticals as borderline topical products could be of crucial importance in the management of different skin challenges related to COVID-19 pandemic.

MATERIALS AND METHODS

Different steps were conducted in preparation of this review. First, literature survey of reported skin symptoms related to pandemic, identification of all factors that affect skin in pandemics (protective measures, disease itself, post-Covid syndrome), selection and classification of symptoms which could be treated with cosmeceuticals. Then, literature survey of studies regarding the effects of relevant cosmeceuticals was done. Relevant data were extracted and reviewed using search engines such as Google Scholar, Science Direct, and PubMed. Appropriate keywords were: "COVID-19", "COVID-2019", "SARS-Cov-2", "skin", "cutaneous manifestations", "maskne", "PPE and COVID", "Hair and COVID", "Pruritus and COVID", "post COVID and skin", "PPE", "cosmeceuticals" etc.

RESULTS AND DISCUSSION

According to our search, skin challenges in COVID 19 pandemics could be divided into three main categories:

1) Cutaneous manifestations of COVID-19 disease itself;

2) Cutaneous symptoms as a result of wearing protective equipment and using disinfectants;

3) Cutaneous symptoms related to the post COVID-19 syndrome.

Our search included articles referring specifically to the skin findings related to the viral infection, to preventative measures (masks, disinfectants) or to post COVID syndrome, which could be treated with cosmeceuticals or where the use of cosmeceuticals is of great importance. The remaining articles were not included since they were either related to dermatology clinical practice or to other topics related to dermatology in this pandemic, where the role of cosmeceuticals was not relevant.

Cutaneous manifestations of COVID-19 disease

The spectrum of manifestations of symptomatic COVID 19 infection ranges from mild to critical. A significant number of reports worldwide concerned the cutaneous manifestations of COVID-19 that precede common acute respiratory symptoms, and the nature of those cutaneous manifestations was described as highly polymorphic. Different classifications were proposed (8 - 11).

Other cutaneous findings included oral lesions, reactivation of viral infections such as herpes simplex virus (HSV) and varicella-zoster virus (VZV) etc. (8, 12, 13). These lesions manifested at various times in relation to the COVID-19 symptoms, which may indicate whether the lesions are virus-induced or are delayed immunological responses to the infection (9).

However, a great heterogeneous variety of skin manifestations is increasingly associated with infection, characterized with multiple postulated pathophysiologic mechanisms and prognostic factors. Therapeutic approach for the different skin manifestations associated with the infection is little explored, including different options such as antihistamines, topical and systemic steroids, low-molecular-weight heparins (14). Cosmeceuticals are not a therapeutic option, although moisturizers could be of help as adjunctive patient care in some cutaneous manifestations (15).

Cutaneous symptoms as a result of protective measures against COVID-19

Cutaneous symptoms as a result of wearing protective masks

Before the COVID era, skin conditions related to the prolonged use of facial masks were documented only in healthcare workers. Besides feeling discomfort, headache, difficulty while concentrating or breathing, widespread mask use in general population nowadays has resulted in more prevalent and widely recognized mask-related skin conditions (16 - 18). Disturbing skin changes are the most reported side effects of wearing masks. According to dermatologists, but also pharmacists in public pharmacies, who became the most accessible sources of professional healthcare advice for patients in overloaded healthcare systems due to COVID-19, people started complaining about skin irritation, skin dehydration, pruritus, greasy skin, skin injuries and, most commonly, acne (18). Hydrating moisturizers containing ceramide/lipid mixtures and barrier creams are recommended in the treatment of dry skin, while acne in coexistence with dehydrated skin became one of the most commonly reported problems connected to protective masks wearing. During the pandemic, even a new term was developed – "maskne", which refers to the acnes caused by the use of masks. The mechanism of their development is still not understood; this symptomatology occurs in individuals with a previous history of acne vulgaris or arise "de novo" (19, 20). Onset of acne after 6 weeks of start of face mask wearing, exacerbation of acne in this area, distinct pattern, referred to as the O-zone and exclusion of differential diagnoses, are clinical criteria currently proposed for maskne (19). However, having in mind the overload of healthcare systems in COVID-19, people usually self-diagnosed this skin issue due to its characteristics and have searched for solutions in pharmacies or on the web. Due to these circumstances, the position and role of public pharmacies in the prevention and management of skin disorders related to COVID-19 pandemic became significant.

It should be emphasized that relevant papers and guidelines recommend cosmeceuticals as the first choice in the management of maskne, confirming their importance in the treatment of this

extremely common skin issue in general population: more than 250,000 Instagram posts have used "maskne" as a hashtag.

Basic recommendation for "maskne" include antibacterial gentle cleansers with a pH between 5 and 7.3 and moisturizers which help maintain a healthy skin barrier. Benzoil peroxide and beta hydroxy acids (salicylic acid) washes or lotions should be used in order to decrease hyperkeratosis and oil concentration in the skin, while topical niacinamide has been found to reduce sebum production alongside anti-inflammatory action while maintaining an intact barrier function (3, 21). Patients should be encouraged to use oil-free products for their make-up and sunscreens and wherever possible hydrophillic serum-based products with sebum-regulating ingredients. Targeted lesional treatment can be achieved using a topical retinoid, benzoyl peroxide cream or azelaic acid suspension 20% (19, 20).

Special attention is on maintaining skin microbiome. It is confirmed that factors such as temperature, pH balance, and skin humidity are significantly affected with wearing masks which all disturb skin microbiome – recently uncovered main actor in acne development. More precise, inflammatory acne were recently related to a loss of diversity of certain phylotypes of bacteria (21).

Changes in the skin microbiota can result also from changes in the superficial sebum composition and level. It should be emphasized that changes in local skin temperatures under the mask affect sebum excretion rate as well as poral occlusion, the latter occurring as a direct result of prolonged local pressure. One study reported a 10% increase in sebum excretion for each degree rise in temperature (3).

Untill now, gentle cleanser, hydrating moisturiser (including optimal ceramide/lipid mixtures with anti-inflammatory ingredients) and barrier creams are the products proposed in restoration of the skin microbiome, which could be beneficial for treatment and prevention of both maskne and dry skin (19, 21). Consumers can recently find various forms of microbiome skin care in all product types, such as cleansers, serums, moisturizers, toners. Different forms of skin care products with pre-, pro- and postbiotics aiming to keep the skin microbiome functional are available on the cosmeceutical market.

The use of a skin barrier cream under facial mask can also be considered, alongside powder formulations that prevent occlusion, absorb excess moisture and contain zinc oxide. Moreover, the significance of mask pressure off-load, shear and friction forces minimisation and skin moisture balance is emphasized in acne management, since cosmeceuticals which contain zinc oxyde could show excellent lubricating and soothing performances (3, 19).

For severe "maskne", the auspices of a dermatologist is required. However, there are no reports supporting the use of isotretinoin or hormonal therapy for this condition so far (19).

Cutaneous symptoms as a result of hand PPE and disinfectants

Due to the increased use of hand PPE (rubber gloves) and the enhanced hygiene, hand skin disorders became very common during the peak of COVID-19 pandemic. According to WHO, hand washing using water and soap for at least 20 seconds or rubbing with hand sanitizer containing a minimum of 60% alcohol, never in an open wound, is recommended to reduce the chance of viral contamination (22, 23).

Excessive handwashing and use of disinfectants (not only alcohol) disrupt skin barrier function and may lead to irritant and allergic contact dermatitis (23). Disinfectants and surfactants from regular soaps penetrate the skin reacting with proteins and lipids which enables the disruption of skin barrier function and further penetration. The result is dry skin prone to inflammation. Beside the type of surfactant, frequency of handwashing is an extremely important factor. Situation is much more complicated in certain groups - a study shows that that 66.1% of health care workers washed their hands over 10 times per day during pandemic (23). On the other hand, in comparison to common soaps, hygiene with alcohol-based sanitizers showed the lowest rates of skin barrier disruption alongside better activity against microorganisms (24). However, the use of both is challenging to skin function and integrity.

Regarding skin disorders connected to the use of protective gloves, they could be attributed to maceration and erosion, which, along with friction and contact with chemicals in latex gloves leads to defects in skin barrier and increased susceptibility to contact dermatitis. An additional finding could be folliculitis and hyperhidrosis. The increase in the risk of skin damage is connected to increased duration of PPE use, as multiple studies have shown (24).

In both cases, emollients containing hyaluronic acid, ceramide, vitamin E as repairing ingredients should be used on hands. Urea-containing emulsions in treating skin rhagades and potent moisturizers before and after wearing PPE are recommended to prevent skin dryness and scales (24, 25). Soaps formulated with milder surfactants should be used for frequent handwash; dexpantenol is also recommended. Cosmeceutical formulated for this purpose should have satisfying sensorial attributes and meet high expectations- they must be absorbed instantly so that the hands are immediately ready for use; they should be non-sticky, non-greasy and quickly relieve the feeling of skin tightness. American Academy of Dermatology stated in public guidelines that skin damages from frequent handwashing could allow germs and increase risk for infection. The importance of use of cosmeceutical moisturizers with mineral oil or petrolatum is emphasized (25, 26).

Cutaneous symptoms related to the post COVID 19 syndrome

Since WHO introduced the term "long COVID", different cutaneous symptoms were reported. A study conducted from September 2020 to July 2021, investigated 104 total cases of "long haulers". Data were collected 1, 3 and 6 months after the patient's hospital discharge. Beside dermatological symptoms such as vesicular exanthema, relapse of seborrhoeic dermatitis and psoriasis, most people reported telogen effluvium and xerosis (27, 28). It was confirmed that COVID-19 infection leads to dyslipidemia in the stratum corneum. Depressed lipid levels (odd chain triglycerides in particular) were identified in participants with a positive clinical COVID-19 diagnosis, with the possibility of an altered microbiome on the skin surface, reduced barrier function and skin health (3).

Another study included 5,891 long haulers, and hair loss was the most commonly reported post-COVID-19 manifestation (2,800; 48%) (28). Due to the interruption of the anagen phase, telogen effluvium is the most frequent and specific dermatological manifestation in patients suffering from "long COVID syndrome" (29).

Therefore, a significant number of long haulers report dermatological conditions that are not life-threating nor require pharmacotherapy, but they have an impact on everyday functioning. Dry skin is usually managed with cosmeceutical moisturizers as the most prescribed products by dermatologists. Hair loss requires complementary strategies to enhance regrowth after post-COVID-19, from psychological support and patient education to the importance of optimal nutrition, supplementation and topical and injectable hair growth stimulators. There is no evidence that cosmeceuticals *per se* could be effective in the management of this condition, although some plant-based actives (proanthocyanidins) were shown as effective as 1% minoxidil in converting mouse hair follicles from telogen to anagen phase (30).

CONCLUSION

Cosmeceuticals first started to stand out on the skin care market more than 30 years ago. In the following years, they became an expanding category of skin care products, and it seems that current pandemic and related skin issues have increased the significance of cosmeceuticals.

Relevant papers and guidelines recommend cosmeceuticals as the first choice in the management of many skin issues connected with pandemic, confirming their importance. Cosmeceuticals could deliver physiologically relevant effects without the use of prescription drugs, which avoids the unwanted effects of drugs, bringing specific benefits. Moreover, as the most available health care professionals, pharmacists can also provide expertise, knowledge, and advice to patients about cosmeceuticals commonly recommended in the management and prevention of some COVID-related skin issues which could aid the limited resources of overloaded healthcare systems in the era of COVID-19.

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Dermatološki izazovi u pandemiji kovida 19: značaj dermokozmetičkih preparata

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SAŽETAK

Uvod. Iako je kovid 19 danas prisutan u blažoj formi, sistemski poremećaji uzrokovani virusom primećuju se na gotovo svim organima. Dermatološke manifestacije posledica su same bolesti, ali i preventivnih mera koje se preduzimaju radi sprečavanja infekcije. Farmakoterapija je uglavnom potrebna samo u težim slučajevima. U radu su predstavljene neželjene pojave na koži povezane sa svim aspektima kovida 19. Cilj je bio da se pruži sveobuhvatan pregled ovih pojava, kao i da se osvetle uloga i značaj koje dermokozmetički preparati imaju u njihovom lečenju.

Metode. U toku pripreme ovog pregleda najpre su prepoznati faktori koji su u pandemiji uticali na kožu (zaštitne mere, sama bolest, postkovid sindrom), a potom izdvojeni i klasifikovani simptomi na koži koji se mogu tretirati dermokozmetičkim preparatima, i to prema relevantnim naučnim radovima i smernicama.

Diskusija. Dermatološki izazovi u pandemiji kovida 19 mogu se podeliti u tri glavne kategorije: 1) kožne manifestacije u vezi sa samom infekcijom; 2) manifestacije nastale kao rezultat nošenja zaštitne opreme i upotrebe sredstava za dezinfekciju; 3) kožne manifestacije postkovid sindroma.

Zaključak. Dermokozmetički preparati, jedinstvena kategorija proizvoda između kozmetike i leka, preporučuju se u svim slučajevima osim kod teških dermatoloških poremećaja povezanih sa kovidom 19. Zauzimaju važno mesto u radu dermatologa, a pandemija kovida 19 potvrđuje njihovu važnost.

Ključne reči: dermokozmetički preparati, kovid 19, pandemija, postkovid, koža