Review Article

Cosmetovigilance: A review of the current literature

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Abstract

The term "pharmacovigilance" defines the activities related to the collection, detection, assessment, monitoring, and prevention of adverse reactions occurring with medications. Recently, the spectrum of "-vigilance" has broadened to include safety of herbal products and cosmetic products as well. "Cosmetovigilance" was introduced as a new term used for defining surveillance carried out by industry to address the safety of cosmetic products. It was first used in literature by Vigan (1997) to refer to the monitoring of cosmetic product safety. Today, it is recognized globally as a concept of public health. For this systematic review, a PubMed search was conducted in July 2018 for the term "cosmetovigilance."

Keywords: Adverse reaction reporting, cosmetics, cosmetovigilance, dermatological

Introduction

The Federal Food, Drug, and Cosmetic (FD&C) Act defines drugs, in part, by their intended use, as "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" and "articles (other than food) intended to affect the structure or any function of the body of man or other animals" [FD&C Act, sec. 201(g)]. In another section, cosmetics are defined by their intended use, as "articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance" [FD&C Act, sec. 201(i)]. The products covered under this definition are skin moisturizers, perfumes, lipsticks, fingernail polishes, eye and facial makeup preparations, cleansing shampoos, permanent waves, hair colors, and deodorants, or any other substance intended for use as a component of a cosmetic product.[1]

There are differences between requirements for cosmetics in the United States and other countries with regard to legal definitions of drugs and cosmetics, restrictions on the use of color additives and other ingredients, and registration requirements. Some products like sunscreens are regulated as cosmetics in Europe, while they are regulated as drugs in the United States.[1,2] According to Cosmetics Directive of European Union, "a 'cosmetic product' by definition is any substance or preparation intended to be placed in contact with the various external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance and/or correcting body odors and/or protecting them or keeping them in good condition."[2]

Even though the term "cosmeceuticals" is used occasionally for cosmetic products with bioactive ingredients purported to have medical benefits, the Federal Food, Drug, and Cosmetic (FD&C) Act does not recognize any such category as "cosmeceuticals."[3] A product can be a drug, a cosmetic, or a combination of both, but the term "cosmeceutical" has no meaning under the law. Based on the intended use and ingredients, some may meet both definitions of cosmetic and drug. Antidandruff shampoos,

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toothpastes with fluoride, antiperspirant deodorants, and moisturizers with sunscreen are examples. Such products must comply with the requirements for both cosmetics and drugs.

The term "pharmacovigilance" defines the activities related to the collection, detection, assessment, monitoring, and prevention of adverse reactions (ADRs) due to pharmaceuticals. An ADR is any response to a drug which is noxious and unintended, including lack of efficacy.[4] Recently the spectrum of "-vigilance" broadened to include safety of herbal products and cosmetic products as well.[5,6]

"Cosmetovigilance" is a term used for the activities related to the collection, evaluation, and monitoring of spontaneous reports of undesirable events observed during or after normal or reasonably foreseeable use of a cosmetic product.[6] It was first used in literature by Vigan (1997) to refer to postmarket surveillance carried out by industry.[7] Cosmetovigilance was initiated by the French health products safety agency as a part of pharmacovigilance system for cosmetics.[8] Today, it is recognized globally as a concept of public health to address the safety of cosmetic products. Figure 1 illustrates the steps for safety monitoring/-vigilance activities.

Methods

In July 2018, a search for the term "cosmetovigilance" in PubMed database yielded in 18 articles. We identified 15 articles related to the topic and 3 articles that were unrelated were excluded. Five more articles and Food and Drug Administration (FDA) websites were included for they were related to ADR reporting with cosmetics.

Results and Discussion

Even though cosmetic products are usually well-tolerated, as seen with medicine, undesirable effects can be seen with cosmetics and toiletries.[9,10] However, the knowledge and identification of these effects are challenging because of the lack of standardized reporting forms and validation of the reports.[9,10] In addition, the absence of well-established cosmetovigilance systems is another limitation.[11] It has been reported that adverse effects of cosmetics and toiletries are underestimated, even when the consumers/patients pursue medical consultation.[12,13]

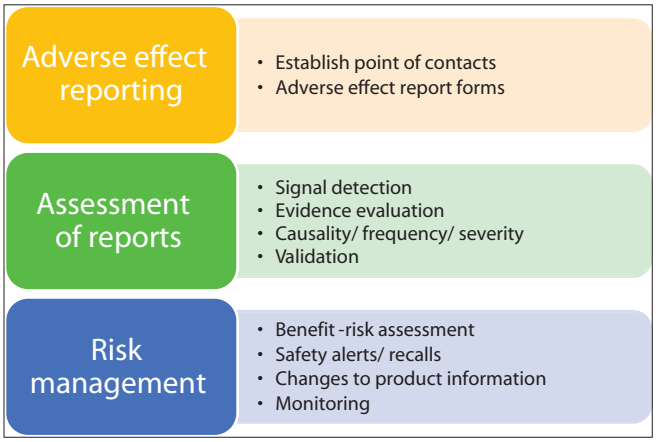

Figure 1: Safety monitoring /-Vigilance activities

USA and Canada

In Canada, consumers and healthcare professionals are encouraged to report unwanted ADR or side effects as per the Natural Health Products (NHP) Regulations, which started in January 2004. The NHP is responsible for assuring that all cosmetic products undergo appropriate licensing, stipulate sufficient evidence for safety and efficacy, require suitable labeling, provide good manufacturing practices, report ADRs, be aware of clinical trials related to the cosmetic products, and be the source of information for product recalls to all consumers. There are report forms, the Cosmetic/Consumer Product Incident Report, specific for consumers and manufacturers. Incident reports must be reported within 15 days of the ADR.[14]

In the United States, there are similar regulations and departments that ensure safety of product use. The following supervise cosmetic products: FDA, The FD&C, Dietary Supplement and Nonprescription Drug Consumer Protection Act, and Guidance for Industry Postmarketing Adverse Event Reporting for Nonprescription Human Drug Products Marketed without an Approved Application. The FDA manages prescription and nonprescription cosmetic products in the country. Similar to the NHP in Canada, the FDA also follows products' labeling, manufacturing, safety and efficacy, ADRs, research, and recalls. In some situations, a cosmetic product may not be FDA-approved but is still FDA-regulated by the FD&C to assure that the product is marketed safely for use. Consumers, healthcare providers, and/or manufacturers are encouraged to report cosmetics-related ADRs to the FDA. The ADRs can be reported to the FDA through MedWatch through an electronic form or by calling the hotline.[15] There is an FDA consumer complaint director to help manage ADR reports. For over-the-counter products, a separate report may be completed, the individual case safety report. In addition, to further address cosmetic safety measures, the United States passed two acts: the Cosmetic Safety Amendment Act in 2012 and the Safe Cosmetics and Personal Products Act in 2013. These two acts encourage more ADR reporting directly to the Secretary of Health and Human Services within 15 days of the ADR.[16]

Europe and Others

One of the first wide-scale studies was published based on the 4-year (2003–2006) reports of four companies' hair coloring products collected from 45 countries. An analysis of undesirable events was performed to determine time course, country effect, and product type. The incidence of allergic contact dermatitis to direct hair coloring products was lower compared with oxidative hair dyes. Interestingly, history of black henna tattoos appeared as a major risk factor for seriousness of allergic contact reactions. This study was the first to identify the risk factors due to cosmetic

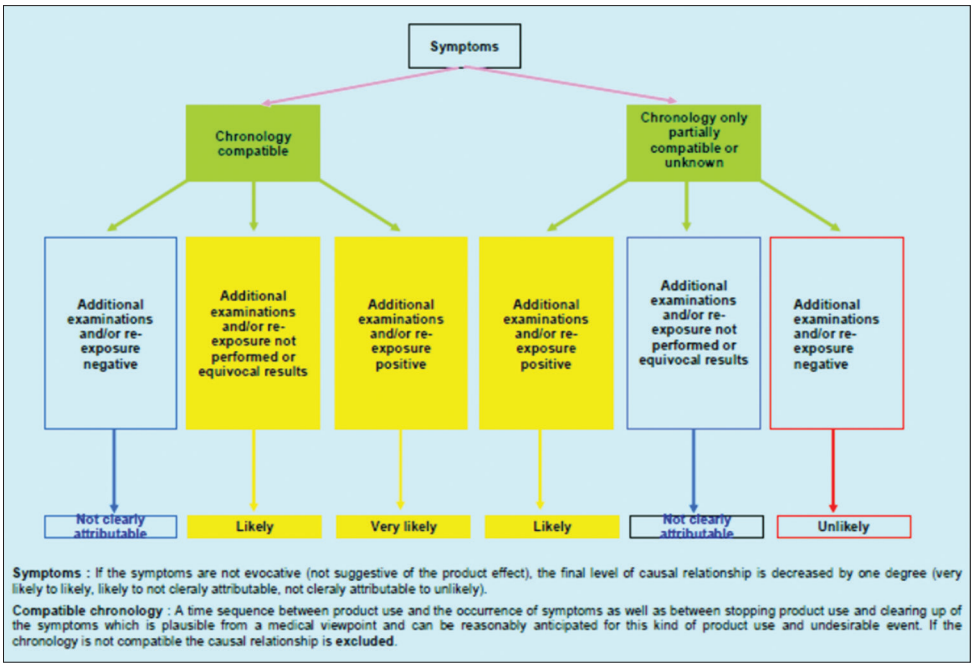

Figure 2: The causality assessment decision tree (with Permission from COLIPA, European Cosmetic, toiletry and perfumery association)

hair coloring products. They concluded that it is important to recognize safety concerns so that warnings to product labels may be revised accordingly.[17]

Another wide-scale study from Europe was published the same year. The data were based on the reports of an industrial company in France.[18] They have established their own vigilance system to surveillance cosmetics and household cleaning products. Between 2005 and 2007, a total of 102,689 consumers contacted the consumer department, including 842 (0.82%) who reported skin reactions. After analysis of the collected data, 0.144 skin reaction cases per million units sold were found to be attributable to cosmetic or household products. This study demonstrated the importance of quality reports and implementation of a structured vigilance system for obtaining reliable data. In 2005, European Cosmetic Toiletry and Perfumery Association (Colipa; currently named as Cosmetics Europe) issued the "Guidelines on Management of Undesirable Event Reports" as a tool for harmonizing industry regarding the collection and evaluation of adverse event reports [See Figure 2]. Post Launch Monitoring and Colipa guidelines aim to assess causality of undesirable effects of cosmetic products on human health.[19-21] The time of onset, duration, and whether it is unexpected or reproducible with rechallenge are key determinants for assessment of causality.[19-21]

As mentioned previously, the distinction between drugs and cosmetics can be confusing because of the lack of standard definitions. The differences in definitions and restrictions on the use of ingredients lead to the different regulatory regimens in the United States and Europe.[1,2] A survey study with 14 countries showed that cosmetovigilance is differently handled in European countries and suggested a need for a formal joint cosmetovigilance system.[22]

Another study from Europe was carried out in Italy.[11] Their findings of this pilot project showed skin reactions represented 96% of the ADR reports due to cosmetic products. The majority of reports were filled out by dermatologists and pharmacists. In many countries, pharmacists are one of the main points of contact in the pharmacovigilance system.[23] For this reason, they can also serve as a good source for cosmetovigilance. In a study conducted in Turkey, pharmacists stated that safety and efficacy were their primary concerns for cosmetics sold in pharmacies, and they expected that manufacturers respond and take responsibility in the case of an ADR.[24]

In Naples (Italy), community pharmacists interviewed 4373 consumers regarding cosmetic adverse events.[25] About 96% of the adverse events were related to cutaneous complaints such as burning and itching. Systemic adverse effects constituted only 4% of all adverse events. Interestingly, 60% of consumers reporting cosmetic-related injury and did not consider any type of consultation. Furthermore, 2.5% of cases who sought medical consultation continued using the product, while taking a drug to treat adverse effects.

A study by Salverda *et al.* evaluated the overview of undesirable effects attributed to cosmetic products in the Netherlands.[26] In addition to the surveys completed by the general practitioners, dermatologists, and consumers, dermatologists also carried out patch tests (with specific batch and ingredients of the associated cosmetic product). A public awareness campaign was launched to promote reporting of undesirable effects. More than 1600 reports were received in 2 years. Severe undesirable effects were claimed in 1%–4% of the cases, with make-up and moisturizers being the most frequently reported products.

In another survey study in Brazil, 38% of the participants declared an ADR with a cosmetic product used in the past 2 years.[27] Soap, shampoo, and deodorants were told to cause the majority of mild to moderate adverse effects. Less than 10% of the ADRs were severe.

In a recent survey study conducted in Ethiopia with 600 participants, 61% of them reported that they experienced adverse effects (i.e. allergic reaction, acne, hirsutism) with the cosmetics they use.[28] The number of products and the frequency of use were found to be associated with ADRs. Even though the results represent a small community, this study is of importance to demonstrate the prevalence and factors for cosmetic-related adverse events.

Another article from India points out that misbranded or spurious cosmetics are commonly reported in India.[29] Furthermore, dermatitis and other ADRs were reported with traditional agents such as kajal and kumkum.

Physician perspective and the role of primary care practitioners in cosmetovigilance

Primary care physicians often see patients with skin complaints. A recent observational study found that 42.7% of visits to primary care physicians were for skin-related issues.[30] Although this included numerous dermatologic diseases, contact dermatitis likely contributed to a substantial percentage of these visits. The American Academy of Dermatology published Guidelines on Contact Dermatitis, which noted that contact dermatitis is responsible for approximately 5.7 million physician visits a year.[31] Contact dermatitis is an inflammation of the skin caused by a substance that has come into contact with it. This can be categorized as either an allergic or irritant dermatitis, meaning the product/substance has produced either an allergic skin reaction or the latter, where it has caused an irritation to the skin. Of the two, irritant dermatitis is far more common accounting for 80% of contact dermatitis.[32,33]

Common allergens that can produce skin reactions include fragrance mix, balsam of Peru, neomycin, thiomersal, formaldehyde, and other preservatives.[34] These ingredients are frequently found in nail polish, perfumes, shampoos, lotions, and cosmetics including foundations, mascara, and lipsticks. A recent study published from Brazil noted that several common allergens and irritants are found in children's skin care products and additionally were labeled as "dermatologist tested" or "hypoallergenic."[35] In the United States, the FDA currently has no regulation on the use of the term hypoallergenic. According to the FDA website on hypoallergenic, hypoallergenic means "whatever a particular company wants it to mean" and "manufacturers of cosmetics labeled as hypoallergenic are not required to submit substantiation of their hypoallergenicity claims to FDA." This allows for unhindered marketing use of the terms "hypoallergenic," "sensitive skin," or "fragrance free" without any consequences.[36] The majority of consumers and physicians are unaware of this and unfortunately have no way of knowing if a certain product has been known to cause an adverse skin reaction, in particular a contact dermatitis. Another study in the United States showed that 89% of children's products labeled as hypoallergenic actually had known allergens or irritants in their formulations.[37]

Cosmetovigilance then falls on the responsibility of the consumer and their physician. Particular care should be advised for those with a history of atopy, asthma, or atopic dermatitis since this predisposes them to contact dermatitis and adverse skin reactions. There are some organizations, such as the National Eczema Foundation, that perform testing on common skin care products and provide product recommendations, which have passed their testing. Unfortunately, until more consumer-friendly databases are easily available and easy to interpret, adverse skin reactions will continue to be common. These adverse skin reactions (contact dermatitis) will continue to produce stress in those who suffer from it and cause financial burden due to missed work, cost of physician visits, and cost of medical treatments.

Although for most medical visits, the ADR is successfully treated and the causal agent identified, notification of the ADR is not reported to the FDA or the manufacturer responsible for the product. The Safe Cosmetics and Personal Care Act of 2013 encourages reports of adverse events to a cosmetic product by providers and consumers and requires reporting by brand owners of the product if there is a serious ADR. Currently, reports can be made through the FDA's MedWatch online system or through a hotline.[15] The data are then collected under the Center for Food Safety and Applied Nutrition adverse event reporting system (CAERS). In December 2016, these data were made available to the public on the FDA's website, with reports dated as early as January 2004.[38] The CAERS database received 3576 reports in 2016, which is up from 445 in 2014.[38] These numbers are underwhelming relative to the number of medical visits made to address contact dermatitis. Using cosmetovigilance in practice can be greatly improved by increasing the awareness of the FDA's reporting system among healthcare professionals. Professionals should take the responsibility along with cosmetic manufacturers to educate patients about the consumer reporting options available. Not only will an increase in reporting bring awareness to possible safety issues with specific products but also it will encourage the FDA to launch investigations and review literature on specific products and their ingredients. Awareness of the now public CAERS database would furthermore increase interest in medical research, improving the overall medical literature and effective treatment implementation of ADRs due to cosmetic products available in the market.

Conclusion

Cosmetovigilance is a new concept of safety monitoring of cosmetic products. It may be considered as an important component of public health activities. As postmarketing surveillance of cosmetics become widespread globally, problems

related to these products can be identified and solved, and thus safety can be achieved.

Family medicine physicians and primary care practitioners have an essential role to recognize ADRs induced by cosmetic products, and thus encourage patients for ADR reporting. Increasing awareness on this new concept will be a valuable remark on global public health.

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Conflicts of interest

There are no conflicts of interest.

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