CLINICAL MANAGEMENT RECOMMENDATIONS

Oxybenzone and Sunscreens: A Critical Review of the Evidence and a Plan for Discussion with Patients

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There has been recent extensive controversy concerning potential environmental and health hazards of oxybenzone (also known as benzophenone-3 and Eusolex 4360). In July 2018, the Hawaii Governor signed a law prohibiting sale and distribution of sunscreens containing oxybenzone.[1] The ban will go into effect in January 2021 and is intended to alleviate possible negative environmental effects of sunscreen chemicals on nearby coral reefs. Although there has been widespread related media attention, there is little definitive scientific research supporting the associated concerns.[1] In addition, some advocacy groups have raised worries regarding potential human health hazards of oxybenzone. Given these controversies, it is critical that dermatologists have a clear understanding of the underlying issues related to oxybenzone in order to effectively counsel their patients. The purpose of this paper is to provide dermatologists with a framework for presenting this issue to patients.

IS OXYBENZONE THE REASON FOR CORAL BLEACHING?

In-vitro experiments have found oxybenzone can cause coral bleaching at concentrations of 33-50 parts per million (ppm).[2] However, these experiments created artificial conditions not reflective of actual marine reef ecosystems. Additionally, they raised oxybenzone concentrations to levels much greater than those found in the ocean. To put this into perspective, water sampled off the coasts of Hawaii and the US Virgin Islands have shown maximum oxybenzone concentrations of 0.019 and 1.4 ppm respectively – materially less than those noted in the *in-vitro* study and therefore unlikely to cause harm.[3]

Environmental changes such as global warming are a more likely culprit in coral bleaching. In Hawaii, water temperature more strongly correlates geographically with coral bleaching than visitor density and associated oxybenzone levels.[4] The increased water temperatures promote viral infection of an important algae, *Zooxanthellae*, that lives symbiotically on coral.[2] The algae are necessary for coral to perform photosynthesis.

Scientists believe that coral bleaching on the Great Barrier Reef has occurred as a direct result of increased water temperatures from global warming.[5] Additionally, the locations where maximal coral bleaching has occurred

do not correlate with where humans populate.[6] There are no *in-vivo* studies that have shown oxybenzone to be directly causative in coral bleaching.

IS THERE DATA TO SUGEST THAT OXYBENZONE IS HARMFUL TO HUMANS?

Oxybenzone has the ability to penetrate the skin, and its metabolic breakdown products are excreted in the urine. Systemic absorption has been observed at a rate of 1% to 2% after topical application.[7] However, the concentrations achieved by cutaneous penetration are too low to cause toxicity.[8]

Very high levels of oxybenzone were associated with estrogenic effects in rats.[9] In that study, immature rats were given extreme doses of oxybenzone orally and found to have increased uterine weights. To reach equivalent systemic concentrations of oxybenzone in humans, one would need to apply sunscreen at the FDA recommended density of 2 mg/cm^2 to 100% body surface area daily for 35 years.[10] Researchers also measured plasma concentrations of oxybenzone and reproductive hormones in men and women after application of 10% oxybenzone, finding no biologically significant differences in hormone levels.[11]

Oxybenzone has also been suggested as a contact allergen. However, a meta-analysis of 64 studies measuring oxybenzone rates of sensitization and irritation found only 0.07% of 19,570 patients had true contact dermatitis to oxybenzone when undergoing patch testing.[12] Another study of 23,908 patients found only 0.9% had a patch-test-proven sunscreen allergy.[13] To date, there have been no clinically significant negative effects of oxybenzone in humans.

WHY IS OXYBENZONE USED IN THE MAJORITY OF U.S. SUNSCREENS?

Since 1978, oxybenzone has been an FDA approved sunscreen agent. Although there are some restrictions and labeling requirements for use in Europe, it is widely used in sunscreens and other consumer products in the US.[14] It has broad-spectrum coverage, successfully filtering UVA (320-440 nm) and UVB (290-320 nm) rays.

Oxybenzone has many advantages over inorganic ingredients (TiO_2 and ZnO). It is photostable, inexpensive, and easily spread on skin. Consumers often prefer sunscreen formulations with organic sunscreening agents due to greater cosmetic acceptability. Although inorganic sunscreens have a relatively flat UV protection spectrum, they have significant disadvantages, including minimal water-resistance, clumping, need for more frequent reapplication, and inability to achieve high SPFs without being cosmetically unacceptable due to deposition of a white cast on the skin. The highest SPF sunscreens often require a combination of both organic and inorganic filters to optimize UV-protection.

ARE THERE OTHER POTENTIAL PROBLEMS WITH OXYBENZONE RESTRICTIONS?

Regular sunscreen usage reduces skin cancer risk.[15] Hawaii has one of the highest rates of skin cancer in the US making it surprising that this state chose to implement this law. As such, the Hawaii Medical Association, many expert dermatologists, and sunscreen manufacturers all opposed the law.[1] Other states may follow Hawaii's lead in banning oxybenzone.

Only 30% of sunscreens will be available to the population in Hawaii leading to a potential increased future skin cancer risk in both residents and visitors.[1] Spray formulations of sunscreen are rapidly becoming the most popular choice of sunscreen users[16] and creating oxybenzone-free versions of these products is difficult due to the inherent physical properties of inorganic sunscreen agents.

Patients are ill informed about sunscreen, including gaps in understanding of concepts such as "sun protection factor", "broad spectrum", and proper techniques of sunscreen application.[17,18] Additionally, little research has been done on patient knowledge of sunscreen composition. Due to this knowledge gap, the most worrisome outcome is that consumers may decide to forgo sunscreen based on unfounded fears that "sunscreen is bad" and thus increase their skin cancer risk.

HOW SHOULD DERMATOLOGISTS RECONCILE THE SCIENCE TO ADVOCATE FOR PATIENTS?

The current state of science does not appear to justify instituting an outright ban on oxybenzone. Misinformation and misinterpretation of studies that were not done in humans (such as those done on rats, *in vitro*, and in artificial marine ecosystems) led to this law.[2,3,9] As dermatologists and physicians, we should strive to be patient centric and continue our focus on lowering skin cancer incidence and mortality.

This is not to say that dermatologists are not sensitive to possible negative effects on the environment. While we encourage further research, we believe that the potential risks to patients by curtailing access to effective sunscreening agents must be seriously considered. A recently published review of the environmental effects of sunscreen ingredients concluded that potential environmental concerns alone should not detract dermatologists from continuing to educate their patients on the importance of sun protection.[19]

WHAT IS A REASONABLE APPROACH TO DISCUSS THIS ISSUE WITH PATIENTS?

Weighing a theoretical risk of coral damage versus a clear benefit from sunscreen usage and then prohibiting patients from obtaining over 70% of sunscreens is not in their benefit. Given this, we suggest the following approach when discussing these issues with patients:

1) There is strong data to support sunscreen usage lowers skin cancer risk.
2) There is laboratory evidence to suggest oxybenzone has negative environmental effects, but these experiments were not representative of real-world conditions and thus results are inconclusive.
3) If a patient is concerned about possible environmental effects, they may use inorganic sunscreens, but they should be counseled about the associated disadvantages.
4) Sunscreens are one part of a total sun-protection package that includes avoiding the midday sun and using sun-protective clothing.
5) The optimal sunscreen is one that patients will use consistently, keeping in mind cost and cosmetic acceptability.

With the media attention given to this topic, public awareness and questions from our patients will continue to increase in magnitude. Using this framework, dermatologists will be more prepared to answer patient questions, dispel

misconceptions, and optimize sunscreen selection.

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