Should Titanium Dioxide–containing Drugs Be Discontinued in Patients with Frontal Fibrosing Alopecia?

Sir,

We read with great appreciation the article published by Aerts *et al*. on frontal fibrosing alopecia of titanium dioxide in 2019.[1] The incidence of this type of cicatricial alopecia, which usually affects postmenopausal women, has increased approximately tenfold over the past decade. Reporting that some sunscreens and cosmetic products may be responsible for the etiology of frontal fibrosing alopecia has caused great concern in dermatologists recommending these sunscreens and in patients using them. Even if patients are not warned about this issue, they access and read these articles on the internet and ask dermatologists questions in this direction. Titanium dioxide is present as a preservative in many drugs used in frontal fibrosing alopecia and other systemic treatments, thus increasing the risk of exposure to this substance. Patients ask their dermatologists about whether these drugs should be avoided.

To answer these questions, we tried to determine titanium dioxide sensitivity in our patients who were diagnosed with frontal fibrosing alopecia based on clinical, trichoscopic, and histopathological findings. For this purpose, patch test with titanium dioxide (Chemotechnique, T-042) was performed on 21 (15 women and 6 men) patients. Six of the female patients are in the premenopausal period. The test results of these patients, whose mean age is 47.14 (age range: 21–68) years, were checked at 48, 72, and 96 hours (according to the guidelines of the British Society of Dermatology), but no positive response was detected.[2] However, the lichenoid reaction may occur early or months or even years after exposure. Therefore, for subsequent readings, patients were instructed on how to check the application sites and to apply to the clinic in case of doubt. However, some late positive reactions may have been overlooked in this study due to non-compliance with our instructions.

In recent years, the sunscreens and some of cosmetic products contain titanium dioxide. A patient with improved frontal fibrosing alopecia has been reported by the removal of this content from sunscreens.[3] In the hair analysis of a different patient, particles containing titanium dioxide were detected.[4] It is suggested that these particles cause a T-lymphocyte-mediated allergic reaction and lead to a lichenoid reaction. However, as in our cases, in eight patients with frontal fibrosing alopecia, no positivity was detected in the patch test with cosmetic products containing titanium dioxide.[5] According to these results, it was thought that titanium dioxide potentiates some contact sensitizers indirectly, not directly. Due to the low sensitivity of the patch test with titanium salts, it is reported that different titanium salts should be used.

It has also been reported that *in vitro* tests such as lymphocyte transformation test or memory lymphocyte immunostimulation method may be used. As there are conflicting results about the relationship between frontal fibrosing alopecia and titanium dioxide, and studies are conducted with a few cases, it is necessary to determine the sensitivity of titanium dioxide in frontal fibrosing patients with *in vitro* tests as well as patch testing. In *in vitro* studies with ionic and nanoparticles, especially ionic forms of titanium dioxide, trigger inflammation.[6] So it is necessary to ask the same question again. Are we, as doctors, trying to treat the inflammation caused by titanium dioxide, which is included in the drugs we give to patients?

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Conflicts of interest

There are no conflicts of interest.

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