

Parabens for allergists

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Dear Editor,

What are parabens?

Parabens are esters derived from para-hydroxybenzoic acid used as preservatives in cosmetics, medicines, personal hygiene and cleaning products, shampoos, and foods. The fungicidal and bactericidal properties of parabens provide protection against microorganisms that may damage product integrity. They are tasteless, odorless, and colorless; furthermore, due to their good availability, efficacy, and low cost, can be combined with other types of preservatives in the same product.¹

Commercially available parabens include methyl paraben (MP), ethyl paraben (EtP), propyl paraben (PrP), butyl paraben (BuP), and benzyl paraben (BeP). Human exposure to parabens occurs via topical contact or intake of products containing parabens.^{2,3}

Due to their water solubility, parabens are the most frequent ingredient in cosmetics and may have a cumulative effect because of continuous dermal exposure.⁴ Human exposure to parabens leads to their wide distribution within the body, being detected in samples from several origins, such as urine, serum, breast milk, placental tissue, and amniotic fluid.⁵⁻⁷

In Brazil, the Brazilian National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária, Anvisa) establishes the allowed maximum concentrations of each paraben in cosmetics, personal hygiene products, and perfumes.⁸

Balbani, Stelzer and Mantovani selected 35 medications, both over-the-counter and prescription drugs, marketed in Brazil, including several antihistamines in liquid form, to investigate labeling information on preservatives, dyes, sweeteners, and flavorings. The most common preservatives found in these medications were MP and PrP (43% and 35.6%, respectively).⁹

Safety and effects of parabens on the body

Although parabens were classified as “generally recognized as safe” by the U.S. Food and Drug

Administration (FDA) and the European Medicines Agency (EMA),¹⁰ their safety has been questioned over the last decades, especially because they can cause endocrinological disorders by changing the activity of endogenous hormones and also hormone synthesis, transport, and metabolism, and by having weak estrogenic and antiandrogenic activity.¹¹ Epidemiological studies showed an association between urinary parabens and adverse health effects, including toxicity in human reproduction, oxidative stress (which may contribute to contact sensitization), immunomodulation, and even breast cancer.¹¹⁻¹³

Urinary parabens, including MeP, EtP, PrP, BuP, and BeP were measured in 436 children in a birth cohort using gas chromatography with tandem mass spectrometry, in order to the association of exposure to parabens with age, weight z-score, height, weight for height, and body mass index. Significant associations were observed only in boys, suggesting that exposure to parabens may impair physical growth in 3-year-old boys. Further prospective studies are warranted to understand the toxicological mechanisms of paraben exposures and potential risk of children.¹⁴

Relationship between parabens and allergic diseases

Reactions to parabens are little frequent and usually irrelevant, and the most identified type are allergic contact dermatitis due to the topical use of cosmetics or medicines containing the product. Among the currently used preservatives, parabens are the least allergenic ones.¹

Exposure to parabens was positively associated with aeroallergen sensitization, an important risk factor for the development, morbidity, and severity of asthma and allergic diseases.¹⁵⁻¹⁷

Anaphylactic reactions to parabens are uncommon, but urticaria and angioedema have been described in individuals with acetylsalicylic acid intolerance.¹⁸

The relationship between exposure to parabens and asthma was examined in a cross-sectional study in children aged from 6 to 18 years, and the findings obtained showed significantly higher odds of aeroallergen sensitization with increased urinary PrP and BuP concentrations.¹⁹

Currently, it is not clear whether parabens induce or aggravate allergies, in addition to contact allergy. A study that examined the relationship between exposure to parabens and prevalence of allergic diseases in Japanese children showed that the prevalence of atopic dermatitis was significantly greater in children with high

urinary concentrations of parabens than in those with low concentrations.²⁰

The association between parabens and asthma morbidity was investigated among children with asthma, and with a prevalence of asthma among 4,023 children in the overall U.S. population that participated in the 2005-2014 National Health and Nutrition Examination Survey. Urinary concentrations of paraben biomarkers BuP, EtP, MP, and PP were analyzed with regard to asthma crises and emergency care visits in children with asthma.²¹

Among children with asthma, no associations were observed between any of the parabens and reports of asthma crises or emergency care visits. However, exposure to MP and PP was associated with greater likelihood of reporting emergency care visits due to asthma in the last 12 months among boys with asthma, although boys had lower concentrations of MP and PP biomarkers. Other studies had previously observed a higher frequency of aeroallergen and food sensitization in boys.²¹

Sexual dimorphism was also reported for pediatric asthma and for emergency care visits, with boys showing higher prevalence of asthma and emergency care visits due to asthma exacerbation, which would bias the interpretation of this association though the action of parabens.^{22,23}

No consistent association was identified between pre-natal and early-life triclosan or paraben concentrations and childhood asthma, recurrent wheeze, or allergic sensitization, but again male individuals are usually at greater risk than female individuals.^{24,25}

Increasing urinary triclosan, MP, and PrP concentrations were associated with increased odds of aeroallergen sensitization and risk of asthma in a representative sample of children aged 6 to 18 years. These chemicals are nonpersistent in the body; therefore, urine concentrations are reflective of exposure at a single time.²⁵

These studies of the relationship between allergic sensitization and asthma are cross-sectional, and these associations do not determine causality. Atopic dermatitis was excluded from some studies. Urinary paraben concentrations vary throughout time, and a single determination may result in misinterpretation. In general, the presence of asthma and eczema was based on information from parents and on a standardized questionnaire, and other environmental exposures, besides parabens, may have interfered with the described observations.^{26,27}

The history of preservatives dates back to the 1930s and, ironically, parabens, which the industry sought to replace with “safer” alternatives, are still the most used biocides in cosmetics and seem to be much less

sensitizing than newer agents. The frequency of sensitivity to this widely used biocide has remained low and notably stable for many decades, despite its extensively and progressively expanding use worldwide.^{26,27}

Conclusion

Parabens are preservatives used in foods, medicines, and cosmetics, being considered safe by the Brazilian regulatory agency and by agencies of other countries. Parabens cause allergic contact dermatitis, and other reactions are rare, despite their growing use. Further studies are warranted to establish some association between parabens and asthma/atopic dermatitis, as well as endocrinological disorders and others.

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