ARQUIVOS DE ASMA, ALERGIA E IMUNOLOGIA

Original Article

Prevalence of sensitization to contact allergens in Brazil

Prevalência de sensibilização a alérgenos de contato no Brasil

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ABSTRACT

Introduction: Allergic contact dermatitis is a subtype of contact dermatitis triggered by immunological mechanisms. Patch testing is the gold-standard diagnostic method, and the screening series used should include the most prevalent and relevant haptens for each population. This study aimed to determine the prevalence of sensitization to the contact allergens of the Brazilian baseline series used in clinical practice among patients with suspected contact dermatitis. **Methods:** This was a cross-sectional observational study of patch tests using the Brazilian baseline series of 30 substances in patients with suspected contact dermatitis. **Results:** Of 2996 patch tests performed, 2054 (68.6%) were positive for at least 1 allergen, and 31.4% were negative for all allergens. The most frequently positive allergens were nickel sulfate (29.9%), thimerosal (16%), cobalt (15.3%), fragrance mix (15.1%), and balsam of Peru (8.6%). **Conclusion:** Nickel was the most common cause of contact sensitization in our Brazilian population. However, in approximately 30% of patch tests, the causative substance was

RESUMO

Introdução: A dermatite de contato alérgica é um subtipo de dermatite de contato, desencadeada por mecanismos imunológicos. O teste de contato é o procedimento diagnóstico padrão ouro, e a bateria empregada deve basear-se em uma série de haptenos mais prevalentes e relevantes para cada população. O objetivo do estudo foi conhecer a prevalência de sensibilização aos alérgenos da bateria padrão brasileira, utilizados na prática clínica, em pacientes com suspeita de dermatite de contato. **Métodos:** Estudo transversal observacional de testes de contato com a bateria padrão brasileira composta por 30 substâncias em pacientes com suspeita de dermatite de contato. **Resultados:** Entre os 2.996 testes de contato realizados, 2.054 (68,6%) foram positivos a pelo menos um alérgeno, e 31,4% foram negativos a todos os alérgenos. Os mais frequentemente positivos foram: sulfato de níquel (29,9%), timerosal (16%), cobalto (15,3%), perfume mix (15,1%), e bálsamo-do-peru (8,6%). **Conclusão:** O níquel permanece como causa mais frequente de sensibilização de contato na

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not identified. Studies on the prevalence of sensitization to contact allergens should be conducted in different populations to assess changes over time.

Keywords: Contact dermatitis, allergic contact dermatitis, nickel, haptens, epidemiologic studies.

nossa população. Entretanto, em cerca de 30% dos testes não foi identificada a substância causadora da doença. Estudos para conhecer a prevalência de sensibilização aos alérgenos de contato devem ser realizados de forma seriada em diferentes populações para avaliar as mudanças ao longo do tempo.

Descritores: Dermatite de contato, dermatite alérgica de contato, níquel, haptenos, estudos epidemiológicos.

Introduction

Contact dermatitis (CD) is a common inflammatory skin disease that affects approximately 20% of the general population.[1,2] It occurs after skin exposure to an exogenous substance, which can be either an allergen or a nonspecific irritant.[3] CD is subdivided into allergic CD (ACD) and irritant CD (ICD), with the latter being more common (up to 80% of CD cases).[1,2] ACD is triggered by a type IV delayed hypersensitivity reaction to a contact allergen in previously sensitized individuals, while ICD is triggered by non-immunological mechanisms.[1] These two types of dermatitis are clinically indistinguishable.

A patch test (also known as an epicutaneous test) is the gold-standard diagnostic method for identifying allergens that cause ACD. Patch testing should be performed according to international guidelines and best practice recommendations.[4] In 2023, the Brazilian Association of Allergy and Immunology (ASBAI) conducted an online survey of 223 associates, and the results showed that 98.7% of them treat patients with CD and 81.2% perform patch tests on their patients.[5]

According to De Groot,[6] approximately 5200 substances have been catalogued as potential causative agents of CD (known as haptens or contact allergens), but it is impractical to test for all of them. The prevalence of sensitization to contact allergens is continuously changing, reflecting both lifestyle changes and new industrial products.[7] In addition to time trends, geographical differences in exposure and sensitization prevalences have been observed.[7]

Given the changing trends of contact allergens, the American Contact Dermatitis Society created the "Allergen of the Year" award in 2000 to draw attention to emerging and under-recognized allergens that require surveillance as well as those that have become obsolete and clinically irrelevant.[8]

Within this context, in the 1980s it was determined that each country should have its own standard battery of regional allergens for systematic screening in patch tests.[9] However, the term "baseline series" (BS) is currently preferred over "standard battery," as the latter is insufficient to diagnose all contact allergies. Patch testing can be complemented to include allergens of local importance, which are determined based on exposure type and personal history.[9]

In 2000, the Brazilian Contact Dermatitis Study Group developed the Brazilian BS (BBS), which includes 30 substances.[10] This series has been a reference for dermatologists and allergists across Brazil since its creation, but it has never been updated.[10] In 2013, the Ibero-Latin American College of Dermatology developed the Latin American BS, consisting of 40 substances and incorporating several emerging allergens and more appropriate concentrations and vehicles. It became commercially available in Brazil as a supplemental series of allergens in November 2020.[11]

The composition of any BS of contact allergens should be reviewed and updated periodically in each country to more accurately reflect changes in exposure and sensitization over time, removing obsolete allergens and including emerging ones.[12]

Decisions about which haptens to retain or remove from the BS should be based on objective data concerning sensitization frequency, hence the importance of identifying the prevalence of positive reactions to contact allergens in the BS, as well as their clinical relevance.[11] Weak allergens with low rates of sensitization but high rates of exposure should be retained or included. Conversely, haptens with high sensitization rates but low clinical relevance should be removed. As a general rule, a contact allergen should demonstrate a sensitization prevalence of at

least 0.5% to 1% in the local population to be included in a BS.[11]

The aim of this study was to determine the prevalence of sensitization to the contact allergens of the BBS used in clinical practice among Brazilian patients with suspected ACD.

Methods

This retrospective cross-sectional observational study was conducted by members of the ASBAI Scientific Department of Contact Dermatitis and 4 training centers for allergy and immunology specialists registered with ASBAI between 2006 and 2021. The 30-substance BBS (FDA Allergenic Ltda.; IPI-ASAC do Brasil) was used for patch testing (Table 1).

A total of 2996 patch tests were performed, distributed as follows: 57 in the Immunology Department of the School of Medicine – Universidade de Passo Fundo, state of Rio Grande do Sul; 829 at Hospital Universitário Pedro Ernesto, affiliated with Universidade do Estado do Rio de Janeiro, state of Rio de Janeiro; 845 in the Unit of Skin Allergy and

Table 1
List of contact allergens from the Brazilian baseline series and positivity in the patch test (N = 2996)

Allergen	N (%)
Nickel sulfate 5%	898 (29.9)
Thimerosal 0.1%	480 (16.0)
Cobalt chloride 1%	457 (15.3)
Fragrance mix 7%	452 (15.1)
Balsam of Peru 25%	258 (8.6)
Potassium dichromate 0.5%	257 (8.5)
Neomycin sulfate 20%	222 (7.4)
Methylchloroisothiazolinone/methylisothiazolinone 0.5%	222 (7.4)
p-phenylenediamine (PPD) mix 0.4%	206 (6.9)
p-phenylenediamine 1%	204 (6.8)
Formaldehyde 1%	184 (6.1)
Carba mix 3%	146 (4.9)
Colophony 20%	93 (3.1)
Paraben mix 15%	90 (3.0)
Epoxy resin 1%	83 (2.8)
Turpentine 10%	83 (2.8)
Ethylenediamine 1%	80 (2.7)
Hydroquinone 1%	79 (2.6)
Promethazine 1%	79 (2.6)
Thiuram mix 1%	77 (2.6)
Benzocaine 5%	74 (2.5)
Quaternium-15 1%	55 (1.8)
Quinoline mix 6%	46 (1.5)
Nitrofurazone 1%	41 (1.4)
Propylene glycol 10%	39 (1.3)
Lanolin 30%	37 (1.2)
p-tert-butylphenol 1%	33 (1.1)
Anthraquinone 2%	30 (1.0)
Triclosan 1%	30 (1.0)
Mercapto mix 2%	29 (0.9)

Immunology at the Dermatology Institute Professor Rubem David Azulay – Santa Casa da Misericórdia do Rio de Janeiro, state of Rio de Janeiro; and 1265 in the Unit of Allergy and Immunology of the Department of Pediatrics and Pediatric Surgery of the São José do Rio Preto School of Medicine, state of São Paulo.

Readings of patch test results were performed at 48 h and at 96 h, according to the International Contact Dermatitis Research Group (ICDRG) guidelines, and scored as follows: (-) negative; (+) faint erythema, few papules; (++) erythema, papules, and vesicles; (+++) intense erythema, papules, and coalescing vesicles.

Results

Of 2996 patch tests performed, 2054 (68.6%) were positive for at least 1 BBS allergen, and 942 (31.4%) were negative for all allergens. The most frequent allergens were nickel sulfate (29.9%), thimerosal (16%), cobalt (15.3%), fragrance mix (15.1%), and balsam of Peru (8.6%) (Table 1). Mercapto mix (0.9%), anthraquinone (1.0%), triclosan (1.0%), p-tert-butylphenol (1.1%), and lanolin (1.2%) showed the lowest rates of positive patch-test reactions.

Discussion

In the present study, 68.6% of the patch tests had a positive reaction. Nickel sulfate was the most prevalent allergen in this sample, followed by thimerosal and cobalt chloride.

Along the same lines, the North American Contact Dermatitis Group (NACDG) patch testing results from 2019 to 2020 showed that, of 4121 patients tested, 69.7% had a positive reaction to at least 1 allergen.[13] They also showed a higher prevalence of sensitization to nickel (18.2%), followed by fragrance mix (12.8%).[13] In a previous study encompassing NACDG patch testing results from 2017 to 2018, nickel was the most prevalent allergen (16.2%), followed by methylisothiazolinone 0.2% aqueous (15.3%) and methylchloroisothiazolinone/methylisothiazolinone 0.02% aqueous (11.0%),[14] an emerging allergen not included in the BBS. The Spanish Research Group on Contact Dermatitis and Skin Allergy (GEIDAC), analyzing sensitization to contact allergens in 11,327 patients, found a higher prevalence of sensitization to nickel, methylisothiazolinone, cobalt, methylchloroisothiazolinone/methylisothiazolinone, and fragrance mix.[15]

Sandrin et al., analyzing a sample of 394 patients for sensitization to BBS contact allergens involved in ACD between 2018 and 2020 in a hospital in Santa Catarina, Brazil, reported a higher prevalence of the following haptens: nickel (33.5%), p-phenylenediamine (PPD) mix (23.2%), perfume mix (22.4%), fragrance mix (22.0%), and cobalt (18.9%).[16] As observed in our study, nickel was the most prevalent allergen, probably due to the population's high exposure to products containing this metal.

Our study has limitations. It was conducted at only 4 research centers, which limits the generalizability of the results to the Brazilian population. However, we included a significant number of tests performed by qualified professionals, thus ensuring their standardized execution and providing an initial overview of the prevalence of contact sensitization to the allergens tested in our study population.

Although our findings align with results for the most common allergens in other international BS, data on emerging allergens are lacking in our population. Since 2020, many Brazilian professionals have adopted the Latin American BS as a more comprehensive and current diagnostic tool than the BBS. The Latin American BS is innovative because it incorporates emerging allergens, similar to other international series, but the BBS remains the initial screening tool for ACD in Brazil and needs to be updated.[17]

It should be noted that some substances, such as anthraquinone, hydroquinone, triclosan, nitrofurazone, promethazine, and turpentine, have been included in the BBS but not in the Latin American, North American, European, or international BS, indicating their limited relevance.[18,19] For instance, promethazine is now rarely used in Brazil; its parenteral form was discontinued in February 2024, although its topical form is still marketed for insect bites and local itching. Photosensitivity cases related to promethazine are well documented, and in these cases, photopatch testing is recommended over conventional patch testing.[19] At present, major international BS do not include promethazine,[13,20] and the European Society of Contact Dermatitis recommends its inclusion in the BS only for photopatch testing.[21]

The antimicrobial nitrofurazone, while widely used in the past, has been replaced by more effective agents for the treatment of ulcers and burns.[22] Triclosan (commercially available as Irgasan) is an effective antibacterial agent against gram-positive bacteria and fungi. However, after risk assessment, experts have recommended discontinuing its use in

products such as hand soaps and cleaning supplies due to its high allergenic potential.[23]

Ethylenediamine is currently included in both the BBS and the North American BS, but not in the Latin American, European, or international BS.[17,18,20] Due to its low prevalence of sensitization (0.8%) and even lower relevance, it may soon be removed from the NACDG BS. As a component of aminophylline, reactions to ethylenediamine were more common in the past. However, aminophylline is no longer recommended in the most recent asthma management guidelines.[24] Regarding thimerosal, patch testing is no longer recommended in BS from several countries, and thus thimerosal was the first to be recognized as a "Nonallergen of the Year" by the American Contact Dermatitis Society in 2002 due to its frequently positive, but often irrelevant, reactions on patch testing (past relevance).[8]

Positive patch test results can be difficult to explain to patients when they lack current relevance, and thus patients often ask: if it has no clinical value, why test for it? Such discussion highlights the need to update the BBS by removing obsolete substances of limited relevance and adding new allergens that are clinically relevant to the Brazilian population.

To address this, the ASBAI Scientific Department of Contact Dermatitis formed a study group in 2022 to revise the BBS. Based on scientific evidence, 18 emerging allergens have been added, 13 allergens with no clinical relevance and a low prevalence of sensitization have been removed, and 10 allergens with a high frequency of positive reactions have been retained; some of them with modified concentrations and vehicles. This new BS of contact allergens will soon be tested in the Brazilian population, and the results will be published in this journal.

Conclusions

Nickel was the most common cause of ACD in our Brazilian population, although other emerging allergens, such as methylisothiazolinone and fragrances, are becoming more frequent. Studies on the prevalence of sensitization to the various ACD allergens are of utmost importance and should be periodically conducted to assess changes over time. This will allow us to update the BS of patch test allergens to better suit the Brazilian population, taking into account new allergens and decreased sensitization to existing ones.

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