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Original Article

Main sensitizing agents involved in allergic contact dermatitis in patients of a hospital in western Santa Catarina, Brazil

Principais agentes sensibilizantes na dermatite de contato alérgica em pacientes de um hospital da região oeste de Santa Catarina

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ABSTRACT

Introduction: Allergic contact dermatitis (ACD) corresponds to 20% of contact dermatitis cases, being the most common type of occupational skin disease and a common cause of consultation with a dermatologist or allergist. **Objective:** To identify the main sensitizing agents involved in ACD at a specialized allergy center in western Santa Catarina, a state in the south of Brazil. Methodology: This retrospective, descriptive, quantitative, and observational study involved the review of medical records of all patients who underwent patch testing for ACD from 2018 to July 2020 in the allergy center. The sensitizing agents evaluated in the patch test followed the standard patch series (including the standard Brazilian patch series, cosmetic series, and regional Latin America series). Frequency analyses were performed for qualitative variables and to assess the prevalence of the main sensitizing agents. In addition, the main agents were correlated with sex and age variables using Pearson's chi-square test. **Results:** The most prevalent sensitizing agents were nickel sulfate (33.5%), PPD mix (23.2%), perfume mix (22.4%), fragrance mix (22.0%), and cobalt chloride (18, 9%). The most prevalent substances were nickel sulfate and PPD mix, which are widely used in patients' daily lives. **Conclusion:** The identification of allergens via patch testing provides patients with an opportunity to reduce ACD caused by the sensitizing agents identified.

Keywords: Allergen, allergy and immunology, eczema, hypersensitivity.

RESUMO

Introdução: A dermatite de contato alérgica (DCA) corresponde a 20% dos casos de dermatite de contato, sendo recorrente em doenças ocupacionais e causa frequente de procura por profissionais dermatologistas e alergistas. **Objetivo:** Identificar os principais agentes sensibilizantes na dermatite de contato alérgica em um centro especializado em alergia do oeste de Santa Catarina. **Metodologia:** Trata-se de um estudo do tipo retrospectivo, descritivo, quantitativo e observacional, no qual se realizou a análise por meio de prontuários médicos de 394 pacientes que realizaram o teste de contato por dermatite de contato alérgica no período de 2018 a julho de 2020 no serviço de referência do oeste de Santa Catarina. Os agentes sensibilizantes avaliados no teste de contato foram conforme as baterias padrão (bateria padrão brasileira, bateria de cosméticos e higiene e bateria regional da América Latina). Foram realizadas análises de frequência para as variáveis qualitativas e avaliação da prevalência dos principais agentes sensibilizantes. Além disso, foram relacionados os principais agentes com as variáveis sexo e idade por meio do teste de Qui-quadrado de Pearson. **Resultados:** Os agentes sensibilizantes mais prevalentes foram: níquel (33,5%), PPD mix (23,2%), perfume mix (22,4%), fragrância mix (22,0%) e cobalto (18,9%). As substâncias mais prevalentes foram o níquel e o PPD mix, que são agentes sensibilizantes usados amplamente no cotidiano dos pacientes. **Conclusão:** A identificação dos alérgenos através do *patch test* possibilita aos pacientes a oportunidade de amenizarem a DCA provocada pelos agentes sensibilizantes encontrados.

Descritores: Alérgeno, alergia e imunologia, eczema, hipersensibilidade.

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Introduction

Contact eczema occurs when the skin is exposed to an allergen capable of provoking irritation or allergy via an inflammatory reaction.[1] Contact dermatitis (CD) accounts for 90% of all occupational skin diseases and is the most common cause of these diseases.[2] Contact eczema is subdivided into allergic contact dermatitis (ACD) and irritant contact dermatitis (ICD), which are classified according to the sensitizing agent involved.[3] ICD is responsible for the majority of CD cases, at around 80%, while ACD accounts for just 20% of cases.[3]

ACD is a disease that is caused by a Gel and Coombs hypersensitivity type IV reaction to an exogenous antigen.[4] According to Brar,[5] there is a sensitization period, during which effector T cells are produced by the body, with the result that an eczematous reaction mediated by memory T lymphocytes occurs 24 to 36 hours after a second exposure to the sensitizing agent.

Allergic contact dermatitis can present as a localized rash and is most commonly seen on the hands and face or is disseminated. During physical examination of a patient, ACD may be detected in an acute or chronic state, in the first of which it will normally present as an erythematous, eczematous, or blistered dermatitis, while in the second state it will present as lichenification, which may be cracked and flaky.[6] Other clinical signs and symptoms may also be found, such as erythema, papules, pruritus, secretions, and blisters.[5] The most common sites of ACD involvement are the hands, face, eyelids, trunk, lips, arms, and scalp.[7] The hands are the most common site of contact dermatitis and nickel, cobalt, fragrances, and rubber additives are the allergens most often responsible.[8]

Allergens are identified using the gold standard for ACD diagnosis, which is patch testing.[5] In a study by Shane et al., the main sensitivity allergens found with patch testing were Peru balsam, cobalt, chrome, formaldehyde, fragrance mixes, nickel, quarternium and thimerosal.[9]

ACD is a common complaint at consultations with specialists in allergy and dermatology.[10] It should be noted that studies demonstrating the epidemiology of contact dermatitis in Brazil are rare and even though occupational dermatitis cases are notifiable diseases, the data cannot be considered trustworthy because of major under-notification.[11] This is because workers tend not to seek medical attention and because of fear of being fired.[12]

Occupational CD can cause workers to be sent home or laid off and its prevalence is estimated at 6.7% to 10.6%.[13] ACD can also impact on daily activities and employment activities, since it can cause erythema, blisters, pustules, hemorrhage, scabbing, flaking, and erosions,[14] in addition to eruptions and intense itching.[1] Patients who develop ACD have their wellbeing compromised and may spend long periods off work because of eczema, significantly impacting them socioeconomically.[2]

Therefore, considering that there are still few studies of the epidemiology of contact dermatitis in Brazil, this study contributes to enabling health professionals to question their patients who work at high risk of contact with sensitizing agents, even those without complaints, helping to make notification more reliable.

The primary objective of this study is to identify the main sensitizing agents of allergic contact dermatitis among patients at a hospital in the West of Santa Catarina, Brazil. It also attempts to identify the main sensitizing agents by age group, in order to compare ACD rates at different ages, and also to record the prevalence of these agents by patient sex.

Materials and Methods

This is a retrospective, descriptive, quantitative, and observational study.

The study analyzed the medical records of all patients who underwent patch testing for allergic contact dermatitis from 2018 to July 2020. The study population was estimated as 1,500 patient medical records, but just 394 medical records met the study inclusion criteria. The study was conducted at a hospital in the West of Santa Catarina state and medical records missing the following data were excluded: age, sex, and site and duration of dermatitis.

Data were collected by searching for International Classification of Diseases (ICD) codes L20, L22, and L232 on the hospital computer system.

The following data were extracted from patient medical records: date of birth; sex; race; region; medications; profession/occupation; weight; height; site and duration of dermatitis; risk factors for ACD (atopic dermatitis); sensitizing agents included in the standard test series (standard Brazilian patch series, cosmetic series, and regional Latin America series) and their respective results. Additionally, the results of

patch tests for specific agents and/or biopsies were also recorded for analysis.

The criteria used for standard test result reading were as recommended by the International Contact Dermatitis Research Group (ICDRG) based on + and – symbols, as follows: (-) negative, equating to intensity 1 in Table 1; (+) discrete erythema with some papules (intensity 2); (++) erythema, papules, and vesicles (intensity 3); (+++) intense erythema, papules, and coalescing vesicles (intensity 4).

Data were collected directly into Epi info 7.0. Statistical analyses were performed using PASW Statistics® for Windows version 20.0 (Predictive Analytics Software, SPSS Inc., Chicago, US). Analyses of frequency were conducted for qualitative variables and prevalence analyses were performed for the main sensitizing agents. The main agents were also correlated with age and sex using Pearson's chi-square test. A 5% significance level was adopted for analysis of the statistical tests.

The ethical principles set out in Resolution 466/2012 were followed and the study was approved in August 2020 by the Human Research Ethics Committee – CEP/UNOCHAPECÓ, decision number 4.232.567.

Results

A total of 394 medical records were identified for patients who had undergone patch tests for sensitizing agents included in the standard Brazilian test series, the Latin American regional series, and the cosmetic series. Majorities of the patients studied were female (71.6%) and had white skin (97.2%), followed by brown (2.0%), yellow (0.5%), and not identified (0.3%).

The age group with the highest prevalence of sensitivity to allergens was from 25 to 48 years (45.9%), followed by zero to 12 years (15.2%), 13 to 24 years (13.7%), and 49 to 90 years (25.1%).

The results observed were used to identify the sensitizing agents with greatest prevalence that were considered to have provoked reactions in the patch tests: nickel (33.5%), p-phenylenediamine (PPD) mix 0.4% (23.2%), perfume mix 7% (22.4%), fragrance mix 14% (22.0%), cobalt 1% (18.9%), triethanolamine 2.5% (17.3%), chrome 0.5% (15.9%), Kathon CG 0.5% (15.6%), paraphenylenediamine 1% (15.4%), and octyl gallate 0.35% (13.9%) (Table 1).

Analysis of the main sensitizing agents by patient sex showed that only nickel was significant ($p = 0.000$). Females had a higher prevalence of positive tests for nickel than males (Table 2).

Analysis of the relationships between the ten main sensitizing agents and age showed that cobalt, paraphenylenediamine, perfume mix, and PPD mix were significant ($p < 0.05$). Among the main sensitizing agents, octyl gallate was prevalent in all age groups, PPD mix was prevalent in the 0 to 12 years group, and fragrance mix was prevalent among those 49 or older (Table 3).

Discussion

In this study, it was observed that the most prevalent agent was nickel 5% (33.5%), followed by PPD mix 0.4% (23.2%), perfume mix 7% (22.4%), fragrance mix 14% (22.0%), cobalt 1% (18.9%), triethanolamine 2.5% (17.3%), chrome 0.5% (15.9%), Kathon CG 0.5% (15.6%), paraphenylenediamine 1% (15.4%), and octyl gallate 0.35% (13.9%).

Boyvat and Yildizhan[15] published a study reporting the results of patch tests in Turkey, showing that the main sensitizing agents found were: nickel (19.6%), chrome (6.5%), cobalt (6%), Myroxylon pereirae resin (Peru balsam) (5%) and paraphenylenediamine (3.7%). As such, 4 of the 5 agents found in that study were also identified as prevalent in the present study.

A study conducted from 2002 to 2007 with 2,076 patients using a basic test series from the British Contact Dermatitis Society found nickel, fragrance mix (FM) I, *Myroxylon pereirae*, cobalt, colophony, PPD, neomycin, thiuram mix, carba mix, and FM II.[16] The high prevalence of nickel reaction found in this study, at 33.5%, confirms the scientific literature. A study conducted with patients from 13 centers in North America also reported that nickel was the most often detected allergen, at 17.5%.[17] Along the same lines, Rubins3 also found that among the patients tested, nickel was identified as the most common allergen.

In addition to being the agent with highest prevalence, nickel was also more often reactive among females (39.8%) and in the age group from 25 to 48 years (37.1%). Rubins[3] also found that the most prevalent allergen causing ACD in females was nickel. One of the reasons for this prevalence is the increased exposure of young females under the age of 18 years to jewelry.[3]

According to Rubins,[3] this early exposure sensitizes children, so that when they come into

Table 1
Sensitizing agents in the standard Brazilian patch series, the cosmetic series, and the regional Latin America series

Sensitizing agent	No reaction n (%)	Reaction n (%)	Intensity of reaction n (%)				Pr
			1	2	3	4	
Anthraquinone (n=291)	286 (98.3)	5 (1.7)	3 (1.0)	2 (20.7)	–	–	1.7
Peru balsam (n=299)	282 (94.3)	17 (5.7)	8 (2.7)	6 (2.0)	3 (1.0)	–	5.7
Benzocaine 5% (n=290)	271 (93.4)	19 (6.6)	9 (3.1)	8 (2.8)	2 (0.7)	–	6.5
Chrome 0.5% (n=327)	275 (84.1)	52 (15.9)	31 (9.5)	21 (6.4)	–	–	15.9
P–tert–butylphenol 1% (n=293)	283 (96.6)	10 (3.4)	7 (2.4)	3 (1.0)	–	–	3.4
Carba mix 3% (n=299)	274 (91.6)	25 (8.4)	8 (2.7)	12 (4.0)	5 (1.7)	–	8.3
Nickel 5% (n=340)	226 (66.5)	114 (33.5)	22 (6.5)	32 (9.4)	49 (14.4)	11 (3.2)	33.5
Cobalt 1% (n=296)	241 (81.4)	55 (18.6)	22 (7.4)	23 (7.8)	9 (3.0)	1 (0.3)	18.9
Terebenthine 10% (n=291)	275 (94.5)	16 (5.5)	7 (2.4)	7 (2.4)	2 (0.7)	–	5.5
Colophony 20% (n=314)	299 (95.2)	15 (4.8)	3 (1.0)	7 (2.2)	5 (1.6)	–	4.7
Thimerosal 0.05% (n=297)	262 (88.2)	35 (11.8)	6 (2.0)	10 (3.4)	17 (5.7)	2 (0.7)	11.8
Ethylenediamine 1% (n=297)	292 (98.4)	5 (1.6)	4 (1.3)	1 (0.3)	–	–	1.7
Thiuram mix (n=318)	305 (96.0)	13 (4.0)	2 (0.6)	8 (2.5)	3 (0.9)	–	4.1
Formaldehyde 1% (n=308)	296 (96.1)	12 (3.9)	7 (2.3)	4 (1.3)	1 (0.3)	–	3.9
Hydroquinone 1% (n=293)	268 (91.5)	25 (8.5)	12 (4.1)	9 (3.1)	3 (1.0)	1 (0.3)	8.5
Triclosan 1% (n=296)	285 (96.3)	11 (3.7)	5 (1.7)	3 (1.0)	3 (1.0)	–	3.7
Kathon CG 0.5% (n=319)	269 (84.3)	50 (15.7)	12 (3.8)	15 (4.7)	15 (4.7)	8 (2.5)	15.6
Lanolin 30% (n=304)	294 (96.7)	10 (3.3)	6 (2.0)	1 (0.3)	3 (1.0)	–	3.3
Mercapto mix 2% (n=307)	293 (95.4)	14 (4.6)	9 (2.9)	4 (1.3)	–	1 (0.3)	4.5
Neomycin 20% (n=320)	289 (90.4)	31 (9.6)	11 (3.4)	10 (3.1)	10 (3.1)	–	9.7
Nitrofurazone 1% (n=293)	284 (97.0)	9 (3.0)	6 (2.0)	2 (0.7)	1 (0.3)	–	3.1
Paraben mix (n=321)	311 (97.0)	10 (3.0)	4 (1.2)	2 (0.6)	4 (1.2)	–	3.1
Paraphenylenediamine 1% (n=330)	279 (84.6)	51 (15.4)	15 (4.5)	16 (4.8)	17 (5.2)	3 (0.9)	15.4
Perfume mix 7% (n=317)	246 (77.6)	71 (22.3)	26 (8.2)	29 (9.1)	15 (4.7)	1 (0.3)	22.4
PPD mix 0.4% (n=293)	225 (76.8)	68 (23.2)	32 (10.9)	27 (9.2)	9 (3.1)	–	23.2
Promethazine 1% (n=294)	280 (95.3)	14 (4.7)	8 (2.7)	3 (1.0)	3 (1.0)	–	4.7
Propylene glycol 2% (n=294)	287 (97.7)	7 (2.30	5 (1.7)	1 (0.3)	1 (0.3)	–	2.4
Quarternium 15% (n=296)	279 (94.2)	17 (5.8)	7 (2.4)	7 (2.4)	3 (1.0)	–	5.7
Quinoline mix (n=290)	281 (96.9)	9 (3.1)	4 (1.4)	3 (1.0)	2 (0.7)	–	3.1
Epoxy resin 1% (n=297)	285 (96.0)	12 (4.0)	6 (2.0)	3 (1.0)	3 (1.0)	–	4.0
Amerchol L–101 (n=291)	284 (97.6)	7 (2.4)	2 (0.7)	4 (1.1)	1 (0.3)	–	2.4
Tonsilamine resin Formaldehyde (n=328)	304 (92.8)	24 (7.2)	10 (3.0)	9 (2.7)	4 (1.2)	1 (0.3)	7.3

Pr = prevalence of positive reactions in the population.
ICDRG intensity 1 = (-) No reaction.
ICDRG intensity 2 = (+) Discrete erythema with some papules.
ICDRG intensity 3 = (++) Erythema, papules, and vesicles.
ICDRG intensity 4 = (+++) Intense erythema, papules, and coalescing vesicles.

Table 1 *(continuation)*
Sensitizing agents in the standard Brazilian patch series, the cosmetic series, and the regional Latin America series

Sensitizing agent	No reaction n (%)	Reaction n (%)	Intensity of reaction n (%)				Pr
			1	2	3	4	
BHT (butyl hydroxy–toluene) 2% (n=294)	288 (97.9)	6 (2.1)	4 (1.4)	2 (0.7)	–	–	2.0
Triethanolamine 2.5% (n=299)	247 (82.5)	52 (17.5)	25 (8.4)	22 (7.4)	5 (1.7)	–	17.3
Bronopol 0.5% (n=297)	282 (95.0)	15 (5.0)	10 (3.4)	3 (1.0)	1 (0.3)	1 (0.3)	5.0
Sorbic acid 0.5% (n=292)	287 (98.3)	5 (1.7)	4 (1.4)	1 (0.3)	–	–	1.7
Chloroacetamide 0.2% (n=290)	285 (98.3)	5 (1.7)	3 (1.0)	2 (0.7)	–	–	1.7
Coconut diethanolamide 0.5% (n=293)	276 (94.2)	17 (5.8)	7 (2.4)	7 (2.4)	3 (1.0)	–	5.8
Chlorhexidine 0.5% (n=295)	286 (97.0)	9 (3.0)	5 (1.7)	–	3 (1.0)	1 (0.3)	3.0
Ammonium thioglycolate 2.5% (n=292)	284 (97.2)	8 (2.8)	4 (1.4)	2 (0.7)	2 (0.7)	–	2.7
Germall 115 2% (n=294)	292 (99.3)	2 (0.7)	2 (0.7)	–	–	–	0.7
Disperse blue 124 0.50% (n=196)	170 (86.7)	26 (13.3)	15 (7.7)	9 (4.6)	2 (1.0)	–	13.2
Caine mix 10% (n=180)	172 (95.6)	8 (4.4)	4 (2.2)	4 (2.2)	–	–	4.4
Palladium 2% (n=179)	161 (89.9)	18 (10.0)	5 (2.8)	8 (4.5)	5 (2.8)	–	10.0
Diazolidinyl urea 2% (n=179)	175 (97.7)	4 (2.3)	3 (1.7)	1 (0.6)	–	–	2.2
Dialkyl Thiourea mix 1% (n=179)	175 (97.8)	4 (2.2)	2 (1.1)	2 (1.1)	–	–	2.2
Fragrance mix 14% (n=219)	171 (78.1)	48 (21.9)	19 (8.7)	12 (5.5)	17 (7.8)	–	22.0
Octyl gallate 0.35% (n=180)	155 (86.1)	25 (13.9)	17 (9.4)	6 (3.3)	2 (1.1)	–	13.9
Methylisothiazolinone 0.02% (n=212)	187 (88.2)	25 (11.8)	6 (2.8)	9 (4.2)	9 (4.2)	1 (0.5)	11.8
Methyldibromo glutaronitrile 0.50% (n=192)	176 (91.7)	16 (8.3)	4 (2.1)	9 (4.7)	3 (1.6)	–	8.3
Paraformaldehyde 1% (n=180)	166 (92.2)	14 (7.8)	7 (3.9)	6 (3.3)	1 (0.6)	–	7.7

Pr = prevalência dos reagentes positivos na população.
Intensidade 1 = nenhuma cruz na leitura dos resultados pela ICDRG. Intensidade 2 = (+) discreto eritema com algumas pápulas pela ICDRG.
Intensidade 3 = (++) eritema, pápulas e vesículas pela ICDRG. Intensidade 4 = (+++) intenso eritema, pápulas e vesículas confluentes pela ICDRG.

contact with nickel again, it provokes allergic contact dermatitis. Moreover, cellphones also contain metals, and nowadays contact with these devices starts early, facilitating onset of ACD.

Another important aspect that should be mentioned is that nickel is involved in orthopedic surgical procedures. According to Nassau and Fonacier,[7] sensitization to nickel increased after joint replacement, since as the metal undergoes wear, free ions are released and deposited in the area around the prosthetic joint. The same authors also explain that nickel can be found in elevated concentrations in some foods, such as chocolate, vegetables, nuts, figs, peanut butter, chocolate spreads, and breakfast cereals.

PPD mix 0.4% contains 3N-phenyl-N-isopropyl-p-phenylenediamine and N-N-diphenyl-p-phenylenediamine, each at 0.2%.[18] The current study observed a 23.2% overall prevalence of positive reactions, which were more prevalent among females (23.4%) and most common in the age group from zero to 12 years (26.3%).

A Brazilian study with 630 patients, 69 of whom had occupational contact eczema, found that PPD mix 0.4% was one of the main allergens linked to occupational contact dermatitis clinical status.[18] Moreover, the same authors state that PPD is primarily used in hair dyes, make-up, the textile industry, and henna tattoos. These uses are more common among women, which coincides with the research findings.

The allergens perfume mix and fragrance mix are combinations of several perfumes and have similar components, which is why they had similar prevalence, at 22.4% and 22.0%, respectively. Each of the two mixes were tested on different numbers of patients, 317 in the case of perfume mix and 219 for fragrance mix.

Additionally, these two sensitizing agents are part of different test series, fragrance mix is part of the regional Latin America series and perfume mix is part of the standard Brazilian patch series. Moreover, Geier and Brans[19] state that the frequency of positive reactions to fragrance mix II has been reducing over recent years.

Table 2
Main sensitizing agents by sex

Sensitizing agents	Sex		p	Pr	
	Female n (%)	Male n (%)		F	M
Chrome 0.5%					
Reaction	36 (15.5)	16 (16.8)	0.766	15.5	16.8
No reaction	196 (84.5)	79 (83.2)			
Cobalt 1%					
Reaction	39 (18.1)	16 (19.8)	0.750	18.1	19.8
No reaction	176 (81.9)	65 (80.2)			
Fragrance mix 14%					
Reaction	30 (19.7)	18 (26.9)	0.240	19.7	26.9
No reaction	122 (80.3)	49 (73.1)			
Octyl gallate 0.35%					
Reaction	15 (11.8)	10 (18.9)	0.212	11.8	18.9
No reaction	112 (88.2)	43 (81.1)			
Kathon CG 0.5%					
Reaction	40 (17.2)	10 (11.5)	0.209	17.2	11.5
No reaction	192 (82.8)	77 (88.5)			
Paraphenylenediamine 1%					
Reaction	33 (14.0)	18 (19.1)	0.241	14.0	19.1
No reaction	203 (86.0)	76 (80.9)			
Perfume mix 7%					
Reaction	51 (22.5)	20 (22.2)	0.962	22.5	22.2
No reaction	176 (77.8)	70 (77.5)			
PPD mix 0.4%					
Reaction	50 (23.4)	18 (22.8)	0.917	23.4	22.8
No reaction	164 (76.6)	61 (77.2)			
Nickel 5%					
Reaction	98 (39.8)	16 (17.0)	0.000	39.8	17.0
No reaction	148 (60.2)	78 (83.0)			
Triethanolamine 2.5%					
Reaction	34 (15.5)	18 (22.5)	0.159	15.5	22.5
No reaction	185 (84.5)	62 (77.5)			

Pr = prevalence of positive reactions by sex, male (M), female (F).

Table 3
Prevalence of sensitizing agents by age

Sensitizing agent	Patients with reactions n (%)	Patients without reactions n (%)	Prevalence	p
Chrome 0.5%				
0-12 years	15 (28.9)	37 (71.1)	28.8	0.038
13-24 years	7 (16.6)	35 (83.4)	16.6	
25-48 years	21 (13.9)	131 (86.1)	13.8	
49 years or older	9 (11.1)	72 (88.9)	11.1	
Cobalt 1%				
0-12 years	8 (22.2)	28 (77.8)	22.2	0.040
13-24 years	4 (10.0)	36 (90.0)	10	
25-48 years	35 (24.2)	110 (75.8)	24.1	
49 years or over	8 (10.6)	67 (89.3)	10.6	
Fragrance mix 14%				
0-12 years	5 (14.2)	30 (85.8)	14.2	0.107
13-24 years	3 (9.7)	28 (90.3)	9.67	
25-48 years	24 (24.3)	75 (75.7)	24.2	
49 years or over	16 (29.7)	38 (70.3)	29.6	
Octyl gallate 0.35%				
0-12 years	1 (5.9)	16 (94.1)	5.88	0.216
13-24 years	1 (3.8)	26 (96.2)	3.70	
25-48 years	16 (17.8)	74 (82.2)	17.7	
49 years or over	7 (15.3)	39 (84.7)	15.2	
Kathon CG 0.5%				
0-12 years	3 (12.5)	35 (87.5)	7.8	0.068
13-24 years	12 (26.7)	33 (73.3)	26.6	
25-48 years	20 (13.0)	134 (87.0)	12.9	
49 years or over	15 (18.3)	67 (81.7)	18.2	
Paraphenylenediamine 1%				
0-12 years	6 (16.3)	31 (83.7)	16.2	0.302
13-24 years	5 (11.2)	40 (88.8)	11.1	
25-48 years	21 (13.2)	138 (86.8)	13.2	
49 years or over	19 (21.4)	70 (78.6)	21.3	
Perfume mix 7%				
0-12 years	10 (26.4)	28 (73.6)	51.7	0.640
13-24 years	7 (15.6)	38 (84.4)	27.8	
25-48 years	34 (22.6)	117 (77.4)	34.8	
49 years or over	20 (24.1)	63 (75.9)	33.3	
PPD mix 0.4%				
0-12 years	21 (56.8)	16 (43.2)	26.3	0.000
13-24 years	11 (26.9)	30 (73.1)	15.5	
25-48 years	23 (16.2)	119 (83.8)	22.5	
49 years or over	13 (17.8)	60 (82.2)	24	
Nickel 5%				
0-12 years	16 (30.2)	37 (69.8)	30.1	0.358
13-24 years	10 (23.3)	33 (76.7)	23.2	
25-48 years	59 (37.1)	100 (62.9)	37.1	
49 years or over	29 (34.2)	56 (65.8)	34.1	
Triethanolamine 2.5%				
0-12 years	2 (5.4)	35 (94.6)	5.4	0.065
13-24 years	9 (21.5)	33 (78.5)	21.4	
25-48 years	32 (21.7)	116 (78.3)	21.6	
49 years or over	9 (12.5)	63 (87.5)	12.5	

Fragrance mix had greatest prevalence in the over 49 years age group (29.6%), which is in line with the findings of a review by Garg, McDonagh, and Gawkrodger,[16] in which fragrance allergy increased with age. Also according to these authors, this rise could be because of cumulative exposure to personal hygiene products and increased use of medications or impaired epidermal barrier function, because of aging.

In the same study by Garg, McDonagh and Gawkrodger,[16] which patch tested 2,076 patients with the British Contact Dermatitis Society basic test series, women predominated in all sensitizing agent age groups. However, in the present study, it was observed that the prevalence of reaction to fragrance mix was higher among males (26.9%) than females (19.7%). Nevertheless, the prevalence of perfume mix reaction was higher among females (22.5%), than males (22.2%).

Fragrances are found in personal hygiene products, cleaning products, and aromatherapy products and the rate of allergic reactions in the general population is in the range of 0.7% to 2.6%.[20] Additionally, fragrances and many other ingredients are defined as commercial secrets by the Fair Packaging and Labeling Act, which explains why many products labelled as hypoallergenic or perfume free contain these fragrances.[7] According to Rubens et al., their study showed that the majority of reactions to ACD occur after exposure to fragrances, preservatives, and hair dyes; which could also be a reason for the higher incidence of ACD among women.[3] While reactions tend to be seen in older women, children also tend to become sensitized by this agent. This takes place not just by exposure of children themselves to the agent, but also by products used by their parents.[21]

Cobalt 1% had a prevalence of 18.9%, and was the second most common metal allergen detected. This allergen was most prevalent among patients aged 25 to 48 years (24.1%), and so both metals – cobalt and nickel – are among the main sensitizing agents in this age group. Cobalt 1% is found in many dental alloys, paints, and pigments used in porcelain and glass.[3] With relation to patient sex, men exhibited a prevalence of 19.8% compared to 18.1% of women, whereas a multicenter study by the Swedish Contact Dermatitis Research Group found a higher proportion of women with positive tests for cobalt 1%.[22]

The allergen triethanolamine is an emulsifier in cosmetic products and is widely used in sunscreen and moisturizers in Brazil, where it had a prevalence of 17.3%, being more common among men and in the 25 to 48 years age group.[23]

Chrome had a higher prevalence of positive tests among males (16.8%) and the 0 to 12 years age group (28.8%). However, the highest proportion of sensitization occurs in adult males and can be attributed to contact with cement and wearing leather footwear.[24]

Kathon CG had a 15.6% prevalence of positive results and was also more common among females (17.2%), while the age group with the highest prevalence of Kathon reactions was 13 to 24 years (26.6%). In comparison, in a Brazilian study conducted in São Paulo with 297 patients, Kathon CG sensitivity had a prevalence of 15.1%, predominantly among women,[25] which results are in line with those of the present study.

Kathon is formed by combining methylisothiazolinone and methylchloroisothiazolinone.[5] Kathon CG is a highly effective preservative and was released onto the market in the 1970s, triggering a global epidemic of ACD caused by this agent.[26]

The main products that contain Kathon are cosmetics, cleaning products, personal care products, glue for use in schools, and wet wipes.[5] Women are probably more affected by allergic contact eczema caused by this allergen because they use more products containing Kathon in their daily lives than men do, which agrees with the results of the present study.

Paraphenylenediamine had a prevalence of 15.4%. It is a component used in permanent hair dyes, temporary henna tattoos, to darken the tone and reduce drying time, leather, furs, textiles, and industrial rubber products.[7] In the present study, it was positive more often in males (19.1%), which may be more related to occupational contact dermatitis, as shown by Nassau and Fonacier,[7] which is also consistent with the age group of greatest prevalence in the current study, which was 49 years or over.

A study that investigated the most prevalent allergens in allergic contact cheilitis found that octyl gallate was in third place.[27] This sensitizing agent was most prevalent in the 25 to 48 years age group and among males, with an overall prevalence of 13.9%. Octyl gallate is used as an antioxidant in cosmetics and medications and by the food industry.[28]

When conducting this study, certain limitations were identified, primarily related to the scarcity of research into the subject, particularly in Brazil. Another

limiting factor is the use of countless different terms for the same sensitizing agents, which makes searching for literature on these products difficult.

It is clear that this study contributes to increasing the body of data on sensitizing agents that cause ACD, describing their relationships with age groups and sex, which could be used to support future research and debates.

Final comments

The main sensitizing agents found in the study population were nickel 5%, PPD mix 0.4%, perfume mix 7%, fragrance mix 14%, cobalt 1%, triethanolamine 2.5%, chrome 0.5%, Kathon CG 0.5%, paraphenylenediamine 1%, and octyl gallate 0.35%. The most prevalent among males were chrome, cobalt, fragrance mix, octyl gallate, paraphenylenediamine, and triethanolamine. Among females, Kathon CG, perfume mix, PPD mix, and nickel predominated. In the 0-12 years age group, PPD mix, perfume mix, and chrome were prevalent. Among the 14-24 years age group, only Kathon CG was prevalent. The predominant agents in the 25-48 years age group were nickel, cobalt, octyl gallate, and triethanolamine. Finally, fragrance mix and paraphenylenediamine were prevalent among patients aged 49 years or older.

Therefore, it is concluded that these test series (standard Brazilian patch series, cosmetic series and regional Latin America series) are important to help patients identify the agent causing their allergic contact dermatitis so they can avoid using these products or becoming exposed to these allergens. It is also suggested that the name of each sensitizing agent should ne standardized to facilitate searching of published data. This would make it possible for patients to avoid agents to which they have become sensitized.

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