



Aouatef Mahfoudh,
Olfa Elmaleel*,
Houda Kalboussi*,
Lamia Bouzgarrou,
Asma Mahfoudh**,
Taoufik Khalfallah,
Najib Mrizak*

Influence of Age on Patch Tests Results

Yaşın Yama Testi Sonuçlarına Etkisi

Abstract

Objective: To assess the influence of age on the patch-test results and to compare the profiles of skin sensitizers according to the age groups.

Methods: It is an 8-year retrospective study involving entire medical records of the patients with allergic contact dermatitis at the Unity of Dermatology and Allergology in the Department of Occupational Medicine, University Hospital of Sousse in Tunisia. Study population was divided into two age groups (group 1: patients <40 years; group 2: patients >40 years). The statistical significance level was taken as $p < 0.05$.

Results: Among the patients, 586 have had at least one positive reaction to the patch-test. Older individuals were 1.1 times more likely to have at least one positive reaction to the patch-test than younger ones. The most common allergens in both groups are potassium dichromate (34.2% vs. 38%), thiuram mix (6% vs. 11%), cobalt chloride (27% vs. 28.8%), balsam of Peru (6% vs. 11.3%) and nickel sulphate (41% vs. 27.3%). A significant variation was noted for potassium dichromate in terms of intensity of skin reaction ($p = 0.00$).

Conclusion: More research is needed to elucidate the physiologic mechanisms of age on the patch-test results and to adapt the European Standard Battery to each age group in term of allergen type and their appropriate concentration.

Keywords: Patch-tests, allergen, dermatitis, age, skin reaction, skin

Öz

Amaç: Yama test sonuçları üzerinde yaşın etkisini incelemek ve yaş gruplarına göre deri duyarlaştırıcılarının profillerini karşılaştırmaktır.

Yöntemler: Bu sekiz yıllık retrospektif çalışma, Tunus, Sousse Üniversitesi Hastanesi, Meslek Hekimliği Bölümü, Dermatoloji ve Alergoloji Ünitesi'nde alerjik kontakt dermatit hastalarının tüm tıbbi kayıtlarını içermektedir. Çalışma popülasyonu iki yaş grubuna ayrıldı (grup 1: <40 yaş hastalar; grup 2: >40 yaş hastalar). İstatistiksel anlamlılık derecesi $p < 0,05$ olarak kabul edildi.

Bulgular: Beş yüz altmış sekiz hasta en az bir yama testine pozitif reaksiyon vermiştir. Yaşlı bireylerin en az bir yama testine pozitif yanıt vermeleri gençlere göre 1,1 kat daha muhtemeldir. İki grupta da görülen en yaygın alerjenler: potasyum dikromat (%34,2, %38), tiuram karışımı (%6, %11), kobalt klorür (%27, %28,8), Peru balsamı (%6, %11,3) ve nikel sülfattır (%41, %27,3). Potasyum dikromat ile deri reaksiyonlarının intansitelerinde belirgin bir varyasyon not edildi ($p = 0,00$).

Sonuç: Yama test sonuçları üzerinde yaş etkisinin fizyolojik mekanizmasının aydınlığa kavuşturulması ve European Standard Battery'yi alerji tipi ve uygun konsantrasyonlar açısından her yaş grubuna uyarlamak için daha fazla çalışmaya gereksinim vardır.

Anahtar kelimeler: Yama testleri, alerjen, dermatit, yaş, deri reaksiyonları, deri

Monastir University Faculty of Medicine, Department of Occupational Medicine and Ergonomics, Monastir, Tunisia

*Sousse Faculty of Medicine, Department of Occupational Medicine, Sousse, Tunisia

**Monastir University Faculty of Pharmacy, Department of Physiology, Monastir, Tunisia

Correspondence/ Yazışma Adresi:

Aouatef Mahfoudh, Monastir University Faculty of Medicine, Department of Occupational Medicine and Ergonomics, Monastir, Tunisia

Phone: +90 216 734 60 35

E-mail: kraimaouatef@yahoo.fr

Submitted/Geliş Tarihi: 05.09.2016

Accepted/Kabul Tarihi: 06.12.2016

Introduction

Patch testing is a well-established method to determine whether sensitization to certain agents has occurred (1). It's considered the gold standard in diagnosis of contact dermatitis (2). About of 3.000 antigens is known to act contact allergic dermatitis. Most of them are small substances with a molecular weight of less than 500 Daltons: called haptens (3). Positive patch test reaction can be influenced by several factors (3-5). Some studies suggest that patch test reactivity depend on age, but this role still poorly clear (6,7). The aim of this study was to evaluate the influence of age on results of patch tests and to compare the profile of most skin sensitizers according to age group in a cohort of 1.019 patients patch tested to the European standard series at the Unit of Dermatology and Allergology in the Department of Occupational Medicine of Sousse in Tunisia.

Materials and Methods

Patients

It is an exhaustive and retrospective study which related to medical folders of patients consulting the Unit of Dermatology and Allergology in the Department of Occupational Medicine of University Hospital, Sousse, in Tunisia. The study was conducted between January 2003 and December 2010. During this period, 1.019 patients with suspected allergic contact dermatitis were patch tested. Patients are excluded if they had applied topical corticosteroids at the test site within 2 weeks: taken systemic corticosteroid more than 20 mg/day or other immunosuppressive drugs within 2 weeks or the skin at test site was abnormal and patients with negative patch test reaction. The European Standard Series Chemotechnique was used, which includes 28 of the most common allergens. For adhesion, we used Finn Chambers on Scanpor tapes applied on the upper back (3,8).

Reactions were evaluated at 48 hours after patch application: which were interpreted according to the recommendation of the International Contact Dermatitis Research Group as follows: (0=negative), (+/-=doubtful), (+=erythema), (++)=papule vesicle formation) and (+++=bullae formation or ulceration) (6).

Only patients having at least one positive skin reaction are included. Study population is divided in two comparison groups: group 1: ≤40 year-older and group 2: >40 year-older. Information collected has included: demographic information (age, gender and atopy), sites of dermatitis, professional characteristics (occupation, length of service) and results of patch tests. Data was analyzed by using descriptive statistic with focus on the so-called MOAHLFA index as the reference instrument for comparison between centers (9).

The correlation was analyzed using Pearson's chi-square test and ANOVA test. The significant level was taken as $p < 0.05$.

Results

Demographics by Age Group: During the study period, 586 patients (57.5%) have had at least one positive reaction. The mean age was 39 ± 12.9 years; ranged from 4 to 86 years. Age group distribution was illustrated in Table 1.

According to age group, patients, distribution varied significantly with gender ($p=0.00$). In the first group, we noted a female predominance (54%) and a male predominance in the second group (64.2%). The rate of atopic dermatitis (AD) lowered significantly with age ($p=0.002$). AD was determined in 29% of younger subjects and 21% of older. The most location of contact dermatitis for both groups was hands (66% and 61.5%). Leg dermatitis among older subject was approximately two times more frequently than younger (27% vs 13%) (Table 2). In this study, the duration of symptoms extended from one to 540 months and didn't vary with age ($p=0.07$).

Common occupations for the two groups' population included unskilled worker (40% and 50%), administrator (12%), health care workers (4%) and machine operative (3%).

Patch Tests Results by Age Group: Older individuals were 1.1 times more likely to have at least one positive patch test reaction than younger individuals. Positive reactions to more than two allergens were noted in half of each group. Specific allergens distributions for two groups are listed in Table 3. The most common ten allergens in the two groups were: potassium dichromate (34.2% vs 38%), thiuram mix (6% vs 11%), cobalt chloride (27% vs 28.8%), balsam of peru (6% vs 11.3%), lanolin alcohol (6%), mercapto-benzothiazole (5% vs 1.9%), paraben mix (6% vs 8%), formaldehyde resin (9.2% vs 10.2%), fragrance mix (7% vs 9%) and nickel sulphate (41% vs 27.3%). Individuals aged 40 years old or less has had the most positive reaction frequency to colophonium (7.8% vs 4.2%) and to lactone mix (5% vs 3.4%). Sensitization to lanolin alcohol and to primin remained at the same level through both groups (6% and 1.6% respectively), whereas frequency of positive reaction to neomycin sulphate have increased from 1.6% in the first age group to 2.3% in the second group.

Table 1. Results of patch tests according to age groups

	Patch tests results				
	Negative reaction		Positive reaction		
	n	%	n	%	
Age group	≤40 years	219	21.5	322	31.6
	>40 years	214	21	264	25.9
Total		433	42.5	586	57.5

Table 2. MOAHLFA characteristics of study population with positive patch tests

	Group 1 (≤40 years)		Group 2 (>40 years)		p
	n	%	n	%	
Male	148	46	95	35.8	0.00
Occupational dermatitis	277	86	235	89.3	NM
Atopic	94	29	56	21	0.00
Hand	212	66	162	61.5	0.02
Leg	45	13.8	71	27	
Face	60	18.8	28	10.6	
Age	177	55	188	45	NM

Significant differences in the positive rate to certain allergens were found between the two age groups particularly to nickel ($p=0.00$); thiuram mix ($p=0.02$), paraphenylenediamine ($p=0.05$), formaldehyde ($p=0.05$), balsam of peru ($p=0.02$), mercapto-benzothiazole ($p=0.04$).

Prevalence of strongly or violently positive reaction (++/+++) was significantly higher in the first age group (77.6%) compared to the second group (70%) ($p=0.03$). For the ten most common allergens, prevalence of positive or strongly positive reaction depended to age group apart nickel sensitization that has remained nearly stable (Table 4). A significant variation of the intensity of skin reaction was noted to potassium dichromate ($p=0.00$).

Discussion

Several studies have shown that allergic contact dermatitis is determined not only by exposure to a particular allergen but also by individual susceptibility (7). In this study, we analyzed the influence of age on contact sensitization by patch-tests.

This study has some limitations. Firstly, it is a retrospective study, therefore certain information may be lacking. Secondly, definition of age group was variable through literature. To reduce this bias, we have adopted the stratification of MOAHLA index and divided study population in two groups, younger (≤ 40 year old) and older subjects (>40 year old) (9).

Table 3. Profile of sensitizer allergen according to age groups

	Age group						
	<40 years		>40 years		Total		p
	n	%	n	%	n	%	
Potassium dichromate, (0.5%, pet.)	110	34.2	100	38	210	35.8	NM
Neomycin sulphate (20%, pet.)	5	1.6	6	2.3	11	1.9	NM
Thiuram mix (1%, pet.)	19	6	29	11	48	8.2	0.02
Paraphenylenediamine (1%, pet.)	14	4.3	21	6	35	8	0.05
Benzocaine (5%, pet.)	8	2.5	12	4.5	20	3.4	NM
Cobalt chloride (1%, pet.)	87	27	76	28.8	163	27.8	NM
Colophonium (20%, pet.)	25	7.8	11	4.2	36	6	NM
Clioquinol (5%, pet.)	1	0.3	0	0	1	0.2	NM
Balsam of peru (25%, pet.)	19	6	31	11.3	50	8.5	0.02
N-isopropyl-N-phenyl-p-PPD (0.1%, pet.)	10	3	11	4.2	21	3.6	NM
Lanolin alcohol (30%, pet.)	19	6	16	6	35	6	NM
Mercaptomix (2%, pet.)	16	5	5	1.9	21	3.6	0.04
Epoxy resin (1%, pet.)	10	3	4	1.5	14	2.4	NM
Paraben mix (16%, pet.)	19	6	22	8	41	6.8	NM
Paratertiarybutyl phenol-formaldehyde resin (1%, pet.)	31	9.6	27	10.2	58	10	NM
Formaldehyde (1%, aq.)	9	2.8	16	6.1	25	4.3	0.05
Fragrance mix (8%, pet.)	23	7	24	9	47	8	NM
Quaternium 15 (1%, pet.)	9	2.8	8	3	17	3	NM
Nickel sulphate (5%, pet.)	132	41	72	27.3	203	34.6	0.00
5-Chloro 2-methylisothiazol 3-one/2-methylisothiazol-3-one (Lyrall) (5%, pet.)	5	1.6	3	1.1	8	1.4	NM
Mercapto-benzothiazole (2%, pet.)	9	2.8	5	2	14	2.4	NM
Lactone mix (0.1%, pet.)	16	5	9	3.4	25	4.3	NM
Hydroxy-methylpentyl-cyclo-hexanecarboxaldehyde (5%, pet.)	5	1.6	3	1	8	1.4	NM
Primin (0.01%, pet.)	5	1.6	4	1.5	9	1.5	NM
Budesonide (0.01%)	4	1.2	1	0.4	5		NM
Kathon CG (0.01%, aq)	6	2	3	1	9	1.5	NM
Pivalate (0.1%, pet.)	3	0.9	2	0.8	5	0.9	NM
1,2-Dibromo-2,4-dicyanobutane (0.3%, pet)	5	1.6	3	1.1	5	1.4	NM

Aq: Aqua, Pet: Petrolatum

In agreement with findings from recent international studies (6,10), we noted a decrease with aging in the frequency of positive patch-tests.

These results may be biased by inclusion of child patients (less than 18 year-old) in the first group. Indeed, several studies have found a highest prevalence of skin positive reaction through child population (3,6). These findings are explained firstly by the increasing of the level of false-positive or non-specific skin reaction in this period of life (11-13), secondly to lack of adapted European Standard Battery for children patients. So that, some authors have suggested that children should be tested with lower concentrations of allergens than adults. Hjorth (14) recommended that patch test concentrations should be adjusted according to the age of patient and that all positive reactions to patch tests should be repeated using the substances in 1/2 strength concentration. Fisher proposed to use 1/2 the standard concentration when patch testing children (15).

The proportion of female patients consulting for eczematous skin lesions was higher in the first group (≤ 40 years) (54%). Similar results were also described by Heine et al. (8), Garg et al. (16) and Yeşilova et al. (17). In general and outside professional activity, house-wife aged less than 40 years old have more family responsibilities with more frequent exposure to alkaline detergents. On the other hand, women wear fake jewelry more frequently during this period.

In our study, the prevalence of atopy decreased slightly with age. Similarly, Warshaw et al. (5) in a comparative study of patch tests results depending on the age conducted among 31942 patients, noted a decrease in the prevalence of atopy with age. This prevalence was 84.4% in younger patients (< 18 years) and 36.4% at subjects aged more than 65 years (5). Active skin disease, such as ADs or even irritant contact dermatitis, disturbs the integrity of the epidermal barrier. So that potential chemical allergens access easily to the immune system and trigger the reaction process of allergic contact dermatitis (18).

The most common site of skin lesions is hand in both age groups, observed in 66% of subjects in the first group

and 61.5% in the second group. Similar results have been described by several authors (7,9,17). In addition, face was more affected in first group and feet were more affected in the second. These findings were consistent with those described by Heine et al. (8).

Type of Allergens and Age: Rate sensitizations to potassium dichromate and to cobalt chloride were slightly increased in the older group. These findings were also reported by Kuljanac et al. (3) and by A. Beliauskienė et al. (9). For certain, it appears to be related to occupational exposure to cement particulars. Indeed, since 2003, the EU Directive has fixed the maximum quantity permissible of hexavalent chromium contained in the cement that should not exceed 2 ppm (19).

Nickel was the leading allergen in adult patients, with a significant influence of age factor on the prevalence of nickel sensitization. To reduce this problem, preventive actions are required at the individual and collective level. In the latter case, accordance to European Union Legislation, members' states are encouraged to reduce the nickel content in jewelry and to use jewelry free of nickel (5).

The second group was more sensitized to common preservative allergens including quaternium-15 and formaldehyde. It reflects an increased exposure to these substances in cosmetic products, personal care products or topical medications in older patients. Similar noticing was reported by Warshaw et al. (5) and Uter et al. (20). Also, we detected an increase in the rate of sensitization to fragrance chemicals at older patients. However, and contrary to results of Uter et al. (20) and Warshaw et al. (5) we noted that the positivity of patch test to colophony allergen was greater in the first age group compared to the second (> 40 years). This may be explained by the predominance of women in this age group, since that colophony is widely used in cosmetics (depilatory waxes, eye shadows, mascaras, foundations, lipsticks, nail polish).

Positive rate of patch tests to neomycin sulphate was doubled in the group of patients older than 40 years. Nethercott et al. found that the odds ratio of neomycin sulphate contact allergy increased significantly with age

Table 4. Intensity of patch tests response according to age groups

	Age ≤40 years				Age >40 years				p
Allergens	±/+		++/+++		±/+		++/+++		
	n	%	n	%	n	%	n	%	
Potassium dichromate	33	30	77	70	14	14	86	86	0.00
Cobalt chloride	47	54.3	40	45.7	38	50	38	50	NM
Nickel sulfate	8	5.6	124	94.4	17	6.4	256	93.6	NM
Thiuram mix	5	26.3	14	73.7	9	31	20	69	NM
Mercapto-benzothiazole	7	81.3	2	18.7	2	40	3	60	NM
Balsam of peru	12	63	7	37	14	44.8	17	55.2	NM
Paraben-mix	6	28.6	9	71.4	6	28.6		71.4	NM
Formaldehyde resin	14	44.4	17	55.6	21	76.5	6	23.5	NM
Fragrance-mix	13	56.5	10	43.5	8	33.3	16	66.7	NM

(odds ratio=1.02; $p<0.001$) (21). These findings are probably the result of the known risk factor of topical antibiotic allergy of stasis dermatitis and stasis ulcers, which usually occur at an advanced age. Also the positivity to benzocaine has increased with age. These findings are also described by other authors (5,9,22). Indeed, benzocaine is an ester local anesthetic. This allergen is found in many topical products, particularly used in the treatment of stasis ulcers and hemorrhoids so that allergic contact dermatitis due to benzocaine has frequently been reported in aged patients (9). A reaction to common rubber accelerators, thiuram mix, was most common allergens in our older population. Similarly, Gupta et al. (23) also found that reactions to rubber accelerators were common in older individuals (second highest group after topical antibiotics) that may be the result of longer exposure for some sources such as gloves, medical devices or shoes what concord with the achievement of leg and feet in older individuals.

Intensity of Allergic Reactions and Age: We found a significant reduction of the overall intensity of patch tests with age: which is synchronous with the change of positives tests rate. In fact, it has been demonstrated an alteration of all precursors of immune response involved in the allergic contact dermatitis with aging. This alteration affects the antigen-presenting cells, especially macrophages, dendritic cells and their drainage to lymph nodes (24). Moreover, based on experimental data, authors demonstrated a decrease in the production of cytokines and interferon- γ by Solana et al. (25) which are the mediators of inflammation in immune allergic dermatitis reaction.

Conclusion

We find no greater difference in positive patch-tests prevalence through two groups. The profile of allergen sensitization and intensity of skin reaction varied significantly with age. These results can be explained by immunologic hypotheses, but more researches are needed to elucidate the physiologic mechanisms of age influence on patch tests results and to adapt the European Standard Battery for each age group in term of type of allergen and appropriate concentration.

Ethics

Ethics Committee Approval: Retrospective study, Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: Olfa Elmaleel, Design: Houda Kalboussi, Data Collection or Processing: Aouatef Mahfoudh, Analysis or Interpretation: Asma Mahfoudh, Aouatef Mahfoudh, Lamia Bouzgarrou, Taoufik Khalfallah, Najib Mrizak, Literature Search: Aouatef Mahfoudh, Writing: Aouatef Mahfoudh.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

- Toledo F, García-Bravo B, Fernández-Redondo V, et al. Patch testing in children with hand eczema. A 5-year multicentre study in Spain. *Contact Dermatitis* 2011;65:213-9.
- Astner S, Gonzalez E, Cheung A, et al. Pilot study on the sensitivity and specificity of in vivo reflectance confocal microscopy in the diagnosis of allergic contact dermatitis. *J Am Acad Dermatol* 2005;53:986-92.
- Kuljanac I, Knežević E, Cvitanović H. Epicutaneous Patch test results in children and adults with allergic contact dermatitis in Karlovac county: a retrospective survey. *Acta Dermatovenerol Croat* 2011;19:91-7.
- Fortina AB, Romano I, Peserico A, et al. Contact sensitization in very young children. *J Am Acad Dermatol* 2011;65:772-9.
- Warshaw EW, Schram SE, Belsito DV, et al. Shoe allergens: retrospective analysis of cross-sectional data from the North American contact dermatitis group, 2001-2004. *Dermatitis* 2007;18:191-202.
- Wöhrl S, Hemmer W, Focke M, et al. Patch Testing in children, adults, and the elderly: influence of age and sex on sensitization patterns. *Pediatr Dermatol* 2003;20:119-23.
- Bordel-Gómez MT, Miranda-Romero A, Castrodeza-Sanz J. Epidemiology of contact dermatitis: prevalence of sensitization to different allergens and associated factors. *Actas Dermosifiliogr* 2010;101:59-75.
- Heine G, Schnuch A, Uter W, et al. Frequency of contact allergy in German children and adolescents patch tested between 1995 and 2002: results from the Information Network of Departments of Dermatology and the German Contact Dermatitis Research Group. *Contact Dermatitis* 2004;7:111-7.
- Beliauskienė A, Valiukeviciene S, Uter W, et al. The European baseline series in Lithuania: results of patch testing in consecutive adult patients. *J Eur Acad Dermatol Venereol* 2011;25:59-63.
- Goh Ch. Prevalence of contact allergy by sex, race, and age. *Contact Dermatitis* 1986;14:237-40.
- Castaneda-Tardan MP, Matiz C, Jacob SE. Contact dermatitis in children a review of current opinions. *Actas Dermosifiliogr* 2011;102:8-18.
- Wetter DA, Davis MD, Yiannias JA, et al. Patch test results from the Mayo Clinic Contact Dermatitis Group, 1998-2000. *J Am Acad Dermatol* 2005;53:416-21.
- Sun CC, Guo YL, Lain RS. Occupational hand dermatitis in a tertiary referral dermatology clinic in Taipei. *Contact Dermatitis* 1995;33:414-8.
- Hjorth N. Contact dermatitis in children. *Acta Derm Venereol Suppl (Stockh)* 1981;95:36-9.
- Fisher AA. Patch testing in children including early infancy. *Cutis* 1994;54:387-8.
- Garg S, McDonagh AJ, Gawkrödger DJ. Age and sex-related variations in allergic contact dermatitis to common allergens. *Contact Dermatitis* 2009;61:46-7.
- Yeşilova Y, Uçmak D, Sula B. Evaluation of patch test results in patients with contact dermatitis. *Dicle Tıp Dergisi* 2011;38:471-6.
- Gittler JK, Krueger JG, Guttman-Yassky E. Atopic dermatitis results in intrinsic barrier and immune abnormalities: implications for contact dermatitis. *J Allergy Clin Immunol* 2013;131:300-13.
- European Commission. Directive 2003/53/EC of the European Parliament and of the Council of 18 June 2003 amending for the 26th time Council Directive 76/769/EEC relating to restrictions on the marketing and use of certain dangerous substances and preparations (nonylphenol, nonylphenol ethoxylate and cement). *Official Journal of the European Union* 2003;178/24-178/28.
- Uter W, Ludwig A, Balda BR, et al. The prevalence of contact allergy differed between population-based and clinic-based data. *J Clin Epidemiol* 2004;57:627-32.
- Nethercott JR, Holness DL, Adams RM, et al. Patch testing with a routine screening tray in North America, 1985 through 1989, III: age and response. *Am J Contact Dermat* 1991;3:198-201.
- Hong MS, Dan JM, Choi JY, et al. Age-associated changes in the frequency of naive, memory, and effector CD8+ T cells. *Mech Ageing Dev* 2004;125:615-8.
- Gupta G, Dawn G, Forsyth A. The trend of allergic contact dermatitis in the elderly population over a 15-year period. *Contact Dermatitis* 1999;41:48-50.
- Imbesi S, Minciullo PL, Isola S, et al. Allergic contact dermatitis: immune system involvement and distinctive clinical cases. *Allergol Immunopathol (Madr)* 2011;39:374-7.
- Solana R, Alonso MC, Pena J. Natural killer cells in healthy aging. *Exp Gerontol* 1999;34:435-43.