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Nickel allergy frequency in a ten-year period in Karlovac County

Učestalost alergije na nikal u desetogodišnjem razdoblju u Karlovačkoj županiji

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Sažetak

The aim of this study was to evaluate the role of nickel sulfate as a cause of allergic contact dermatitis. We revised the clinical records of out-coming patients with allergic contact dermatitis (ACD) and atopic dermatitis (AD) clinical diagnosis at the Department of Dermatology and Venerology of Karlovac General Hospital during the 1994–2005 study period. There were 2828 patients, f: 2033 (71.9%), m: 795 (28.1%) ranging from 7-81, mean age 36. The epicutaneous patch test with 5% nickel sulfate (Institute of Immunology, Zagreb, Croatia) was done. Out of all patients (2828), 373 (13.1%) showed positive epicutaneous patch test reaction to nickel sulphate. Taking into consideration gender, out of all female patients, the nickel positive patch test was recorded in 11.7% patients, while the result in the males was 1.4%. A statistical difference between positive results in females and males was significant ($p < 0.05$).

In order to determine the importance of atopic constitution in nickel sensitivity, patients were divided into two groups: 1. Patients with ACD: 2513 patients, f: 1806 (71.8%), m: 707 (28.2%), ranging from 8-81, mean age: 39.2, 2. Patients with AD (according to Hanifin and Rajka criteria, 1982 (5): 315 patients, f: 227 (72.1%), m: 88 patients (27.9%), ranging from 7-78, mean age: 36.3.

ACD patients in the first group resulted in 332 positive tests (13.2%), while in the second group (atopic patients) 41 resulted positive (13.0%). The difference is not statistically significant ($p > 0.05$).

It is concluded that nickel is the most frequent allergen which affects the younger female.

Atopic constitution does not have any influence on nickel sensitivity. It is equally frequent in persons with and without atopic constitution.

Key words: nickel allergy, epicutaneous test, allergic contact dermatitis, atopic dermatitis

Summary

Cilj rada bio je procjena uloge nikla u nastanku kontaktnog alergijskog dermatitisa (KAD). Obrađeni su rezultati epikutanog testiranja s 5% nikal sulfatom (Imunološki zavod, Zagreb), tijekom 1994.-2005. godine, bolesnika s KAD-om i atopijskim dermatitisom (AD). Od ukupno 2828 bolesnika uključenih u studiju, ž: 2033 (71,9%), m: 795 (28,1%), starosti od 7 do 81 godine, prosječne starosti: 36,6 godina; 373 (13,1%) bolesnika imalo je pozitivan epikutani test na nikal. S obzirom na spol, od svih osoba ženskog spola uključenih u studiju 11,7% imalo je pozitivan epikutani test na nikal, dok je u osoba muškog spola pozitivan epikutani test bio u 1,4% bolesnika, što je statistički značajna razlika ($p < 0,05$)

U cilju određivanja značenja atopijske konstitucije u nastanku senzibilizacije na nikal, pacijenti su bili podijeljeni u dvije skupine: 1. bolesnici s KAD-om: 2513 bolesnika, ž: 1806 (71,8%), m: 707 (28,2%), dobi od 8 do 81 godine, prosječne dobi: 39,2 god., 2. bolesnici s AD-om (prema kriterijima Hanifin i Rajka, 1982 (5): 315 bolesnika, ž: 227 (72,1%), m: 88 bolesnika (27,9%), dobi 7-78 godina, prosječne dobi: 36,3 god.

U prvoj skupini (bolesnici s KAD-om) bila su 332 pozitivna testa (13,2%), a u skupini 2 (bolesnici s atopijom) bio je 41 pozitivan test 13,0%. Razlika nije statistički značajna ($p > 0,05$).

Zaključili smo da se alergija na nikal najčešće javlja u mlađih osoba ženskog spola.

Atopijska konstitucija nema utjecaja na pojavu senzibilizacije na nikal. Ona se javlja s jednakom učestalošću u osoba s atopijskom konstitucijom i bez nje.

Ključne riječi: nikal, alergija, epikutani test, kontaktni alergijski dermatitis, atopijski dermatitis

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Introduction

Allergic contact dermatitis (ACD) is an inflammatory reaction of the skin that follows percutaneous absorption of the antigen from the skin surface and recruitment of previously sensitized, antigen-specific T-lymphocytes into the skin.[1] The causes of ACD are usually small chemical substances which must bind carrier protein to become a complete antigen.[2] It is a classical delayed hypersensitivity, or type IV immunologic reaction. The reaction can be thought as occurring in two phases, initially sensitization and then elicitation response.[2] When the antigen contacts the skin, it is processed and presented with HLA-DR on the surface of Langerhans´ cells,[2] which act as antigen presenting cells in the skin. They present antigen-HLA-DR complex to the helper T cells. The next step is the antigen-HLA-DR complex interaction with T cells. It leads to the proliferation of specific T cell clones that circulate through the body and back into the skin.[2] Although sensitivity to allergens is found in about 10% of the adult population,[2] it is equally as likely in infancy as in adulthood, and represents 20% of all cases of dermatitis in children.[3] Nickel allergy is the most common contact allergy. A hundred years ago it was an occupational disease that mainly affected men.[4] To become sensitised to nickel, direct and prolonged skin contact with items that release nickel ions is required.[4] Nickel is found in many metallic items either electroplated or as an alloy, e.g. costume jewellery, wearing apparel, coins, keys, tools, utensils, instruments, metal parts of furniture, batteries, machinery parts etc.[2] Increased risk of occupational nickel allergy can be found in some professions, e.g. hairdressers, electronic workers, machinists, mechanics etc. The aim of this study was to evaluate the role of nickel allergy in ACD and atopic dermatitis (AD) patch tested patients.

The study was done at the Department of Dermatology and Venerology in Karlovac General Hospital, Karlovac, Croatia, during the 1994-2005 study period.

Material and methods

We revised clinical records of out-coming patients with clinical diagnosis allergic contact dermatitis and atopic dermatitis at the Department of Dermatology and Venerology in Karlovac General Hospital during the 1994-2005 study period. 2828 patients, f: 2033 (71.9%), m: 795 (28.1%), range 7-81, mean age: 37.6, were included in the study. The epicutaneous patch test was done with 5% nickel sulfate (included in standard series of contact allergens) made at the Institute of Immunology in Zagreb, Croatia. All patients were divided in two groups: 1 – patients with clinical diagnosis ACD and 2 – patients with clinical diagnosis AD, according to Hanifin and Rajka criteria.[5] The ACD group consisted of 2513 patients, f: 1806 (71.8%), m: 707 (28.2%) range: 8-81, mean age: 39.2, while the AD patients group consisted of 315 persons, f: 227 (72.1%), m: 88 (27.9%), range 7-78, mean age: 36.3 years (Table 1).

The test substance was applied on the upper part of the patients' back, on clinically uninvolved, untreated, and without tape stripping skin with adhesive strips for patch test (Curatest, Lohmann-Rauscher, Germany). All patients were free of oral antihistamines, steroids and immuno-suppressive drugs. The patch test was removed and reactions were evaluated after 48 h and 72 h. Grading of negative (-) to positive (+ to ++++) patch test was according to the International Contact Dermatitis Group (ICDGR) rules.[6]

Table 1. Patients involved in study according to clinical diagnosis
Tablica 1. Pacijenti uključeni u istraživanje prema kliničkim dijagnozama

Clinical diagnosis *Klinička dijagnoza*	Females (%) *Žene*	Males (%) *Muškarci*	Total (%) *Sveukupno*
ACD / *KAD*	1806 (71.8)	707 (28.2)	2513 (88.1)
AD	227 (28.2)	88 (71.8)	315 (11.9)
Total / *Sveukupno*	2033 (100)	795 (100)	2828 (100)

ACD: Allergic contact dermatitis
KAD: kontaktni alergijski dermatitis

AD: Atopic dermatitis
AD: atopijski dermatitis

Statistical data analysis was performed by using chi-square (χ^2) test. All statistical values were considered significant at the p-level of 0.05.

Results

Out of all patients (2828), 373 patients (13.1%) showed positive epicutaneous patch test reaction to nickel sulfate. According to gender, out of all females patients 333 positive results (11.7%) were recorded, while 40 male patients showed positive results (1.4%) to nickel sulfate (Table 2). In the patients group with ACD, 332 (13.2%) patients were positive to the nickel sulfate; f: 301 (90.6%), m: 31 (9.4%), while in the AD group 41 (13.0%) patients were positive; f: 32 (78.1%), m: 9 (21.9%) (Table 3). According to age, maximally positive results were recorded in 20-50 year-old patients. In female patients the most positive results were recorded between 21-40 years of age, while in the male patients between 30-50 years of age.

Discussion

Anamnesis, clinical features and epicutaneous patch test are very important steps in the identity of specific causative allergen in allergic contact dermatitis.[7] In the ACD, the inflammatory process is caused by the type IV (cell mediated reaction) reaction occurring in sensitized individuals after renewed contact with the antigen. Contact dermatitis accounts for 4-7% of dermatological consultations.[8]

Table 2 . Nickel positive epicutaneous patch test reactions according to sex
Tablica 2. Pozitivni rezultati reakcija epikutanog testiranja prema spolu

Sex *Spol*	Ni + (%)	Ni - (%)	Total (%) *Sveukupno*	p < 0.05
F/*Ž*	333 (11.7)	1700 (89.3)	2033 (100)	SR *ZR*
M/*M*	40 (1.4)	754 (98.6)	795 (100)	
Total *Sveukupno*	373 (13.1)	2455 (86.9)	2828 (100)	

F: Female M: Male SR: Significant result (p < 0.05)
Ž: žene M: muškarci ZR: značajni rezultati

Ni +: Nickel positive epicutaneous test Ni -: Nickel negative epicutaneous test
Ni +: pozitivan epikutani test na nikal N i-: negativan epikutani test na nikal

Table 3 Nickel positive epicutaneous test according to clinical diagnosis
Tablica 3. Pozitivini rezultati reakcija epikutanog testiranja prema kliničkim dijagnozama

Clinical diagnosis *Klinička dijagnoza*	Ni + (%)	Ni – (%)	Total (%) *Sveukupno*	p > 0.05
ACD	332 (13.2)	2181 (86.8)	2513 (100)	NSR *NR*
AD	41 (13.0)	274 (98.6)	315 (100)	
Total *Sveukupno*	373 (13.2)	2455 (86.8)	2828 (100)	

Ni +: Nickel positive epicutaneous test Ni -: Nickel negative epicutaneous test
Ni +: pozitivan epikutani test na nikal N i-: negativan epikutani test na nikal

ACD: Allergic contact dermatitis AD: Atopic dermatitis
KAD: kontaktni alergijski dermatitis AD: atopijski dermatitis

NSR: Not significant result (p > 0.05)
NR : neznačajni rezultat

Today, about 3000 antigens are known to act as contact allergens. Most of them are small substances with a molecular weight of less than 500 daltons called haptens.[9] They bind to a carrier protein via covalent bounds or, in the case of metals, like nickel and cobalt, form a complex with protein.[9] The configuration of the conjugate, a type of binding, and other unknown factors determine the antigenicity.[3,9]

Nickel sulfate is the allergen with the most tested positive reactions in the USA, appearing in almost 10% of the epicutaneous tests and is considered relevant in about 75% of cases.[10] It acts as the most common allergen.[4]

In contact with skin, nickel metal oxidized to form soluble, stratum corneum diffusible compounds which may penetrate the intact stratum corneum, presumably by the intercellular route, have a potential to elicit allergic reaction.[11] In the Czech Republic, 12,058 patients with suspected ACD were epicutaneously patch tested,[12] and the most frequent allergens were metals (22.9%), especially nickel sulfate (13.8%). The North American Contact Dermatitis Group patch test results during the 2001-2002 study period showed nickel sulfate as the top allergen (16.7%).[13] Prevalence of nickel allergy varies from 0.8% to 2.2% in males and 8-11.1% in females.[14-16]

During the 1994-2005 study period, 2828 patients with ACD or AD were involved in our study. Out of all patients, 373 patients showed clear cut positive epicutaneous patch test to nickel (13.1%). According to gender, there was a statistical difference (χ^2 : 43.7; $p < 0.05$) between males (1.4%), and females (11.7%). The results are in accordance with the results mentioned in earlier studies.[12,14-16] The conclusions that can be drawn from these studies regarding the occurrence of nickel allergy in the general population are limited since the access to dermatologists, types of patient, and indications for patch testing varies.[4]

The most often affected patients in our study were younger females (21-40 years old), and it was also recorded by the other authors.[4,12,17]

There is a big contradiction in medical literature regarding the relationship between atopy and contact hypersensitivity.[18] Some results showed less frequent positive patch tests in atopics than in non-atopics[19,20] while some researches found significantly more frequent positive patch test results in atopics than in non-atopics.[21]

The recent study of Spiewak in 2005, did not show a statistical difference in contact sensitivity between atopic and non-atopic patients.[18] In our study of nickel allergy a statistical difference in allergy to nickel between atopic and non-atopic patients was not recorded (χ^2: 0.000007, $p > 0.05$).

It is concluded that nickel is the most frequent allergen as cause of ACD, mainly affecting the younger female patients. Atopy does not promote and does not prevent nickel sensitivity.

Conclusion

Nickel is the most frequent allergen as a cause of allergic contact dermatitis, and predominantly affects younger female persons because of a higher exposure[17] and wearing nickel jewellery. Despite the controversy of the role of atopy in contact sensitization, our results showed that atopy does not promote and does not prevent sensitization to nickel. It is the most common contact allergen with equal frequency in atopic and non-atopic subjects.[22]

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