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A gender-specific approach to occupational allergic contact dermatitis

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Summary

Background A gender-specific approach has been claimed in most diseases. However, data on differences between men and women in occupational allergic skin diseases are limited. This retrospective study aimed to evaluate gender differences in occupational allergic contact dermatitis (OACD).

Methods A retrospective study on OACD was performed in male and female workers in Italy and Tuscany. Cases were collected from the Italian National Institute for Insurance against Accidents at Work (INAIL) database.

Results Data from a total of 1555 patients (58% men and 42% women) with OACD were reported to INAIL in Italy over the 5-year span from 2014–2018. The most common sectors were industry and crafts

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in men, and services and public administration in women. The haptens most frequently involved were cement followed by epoxy resins in men, while hair dyes and rubber additives were identified in women. *Conclusion* Gender-distribution in OACD reflects differences in occupations with respect to men and women as evidenced by working sectors and haptens involved in the pathogenesis.

Keywords Allergic contact dermatitis \cdot Occupational exposure \cdot Gender \cdot Hairdressers \cdot Occupational diseases

Abbreviations

CPD Regional Polydiagnostic Center

- INAIL National Institute for Insurance against Accidents at Work
- OACD Occupational allergic contact dermatitis

Introduction

In the workplace both extrinsic and intrinsic factors may contribute to the development of diseases, but, among all, gender plays a relevant role. The European Agency for Safety and Health at Work (EU-OSHA) actively works to ensure a gender-sensitive approach in policies and actions in order to prevent occupational diseases [1, 2]. The principle of gender mainstreaming (i.e., "the systematic consideration of the differences between the conditions, situations and needs of women and men"), first defined in 1996, became an established part of European Union policy in 2003 and it has been implemented into the occupational safety and health system at different levels from research to monitoring [1]. By acknowledging the strategy of the European Commission, the Italian Legislative Decree 81/2008 stated that risk assessment in the workplace must consider gender differences [3] and the

Permanent Advisory Committee for health and safety at work is in charge of promoting such considerations together with gender-specific preventive measures for all workers [4].

In the last 5 years (2014-2018), 212,024 occupational diseases in men have been reported to the Italian National Institute for Insurance against Accidents at Work (INAIL) and 82,033 in women [5]. Although in 2018 the Italian employment rate was 67.5% for men and 49.6% for women, 73% of notifications of occupational diseases were in men and only 27% in women [5, 6]. Because this wide gender gap in reporting occupational diseases has an impact on prevention strategies, further evidence is needed to elucidate differences between men and women in occupational diseases. Gender has been proven to be a biological variable that affects innate and adaptive immunity [7, 8]. Furthermore, gender has emerged as a valuable factor in medical education and clinical practice [9]. Raulf et al. have shown that in Germany occupational skin diseases are more frequent in women, but the distinction between allergic and irritant dermatitis was not possible because of lacking differentiation in the records [2].

The present study examined gender differences in occupational allergic contact dermatitis (OACD), a chronic inflammatory immune-mediated condition that is one of the most common work-related skin diseases and a major health problem [10–12]. In addition, we evaluated whether gender differences in the same working sectors, particularly in those where women and men are exposed to the same chemical risk factors, e.g., hairdressers, were present.

Materials and methods

Setting and patients

Cases of occupational allergic contact dermatitis (OACD) reported in Italy from 1 January 2014 to 31 December 2018 and cases of OACD diagnosed in Tuscany (a region in central Italy) from 1 January 2012 to 31 October 2019 were collected from the INAIL national database and INAIL Regional Polydiagnostic Center in Florence, Tuscany, Italy (INAIL CPD Florence) dataset, respectively. INAIL is the Italian workers compensation authority, a public nonprofit entity whose role is worker protection through preventive actions at the workplace, medical services, and financial assistance. In Italy, all cases of occupational disease must be reported by clinicians to INAIL via the disease's certificate. Occupational diseases notified in Italy are collected by INAIL and data of a 5-year span are made publicly available every 6 months [13]. For every notified case, the following items are registered: date of detection (i.e., when the information was recorded and extracted from the archives), date of record, date of definition (the date of administrative definition), date of death because of the occupational

disease, site of notification (indicates the district where the case was treated), gender of the worker, place of birth, working sector and subsector, notified disease (according to World Health Organization [WHO], International Classification of Diseases 10th Revision [ICD]) and causal agent (the agent, processing or exposure that can be the cause or contributing cause of the disease). All data were de-identified and tracked using a code number. The following ICD-10 codes were extracted from the records: L23 (allergic contact dermatitis), L23.0 (due to metals), L23.1 (due to adhesives), L23.2 (due to cosmetics), L23.3 (due to drugs in contact with skin), L23.4 (due to dyes), L23.5 (due to other chemical products), L23.6 (due to food in contact with the skin), L23.7 (due to plants, except food), L23.8 (due to other agents), L23.81 (due to cat or dog dander), L23.89 (due to other agents), L23.9 (unspecified cause). Irritant contact dermatitis was not considered. The INAIL CPD Florence dataset is a personal archive of one of the authors (MCA) and collects all notified OACD cases in Tuscany, Italy, since May 2005. The archive has been digitized since 2012. For every notified case, the following items are recorded: gender, age at visit, age at diagnosis, age at beginning of exposure, date of visit, date of diagnosis, date of beginning of exposure, site of notification, occupation, eczema location, patch test results (baseline series and additional series), family and personal history of atopy (allergic asthma, allergic rhinitis and/or conjunctivitis, and atopic dermatitis), and comorbidities. All data were de-identified and tracked using a code number. Cases of OACD in hairdressers were retrieved from the INAIL CPD Florence dataset.

Patch test

All hairdressers were tested with the Italian baseline series recommended by the Italian Society of Allergological, Occupational and Environmental Dermatology (SIDAPA) in use over the years and with the hairdressing series (Supplementary Table 1). In addition, in those patients with medical history suggestive of contact sensitivity to rubber personal protective equipment, patch testing with rubber series in use at INAIL CPD Florence was performed (Supplementary Table 1). Van der Bend Chambers (Van der Bend B.V., Brielle, The Netherlands) and haptens from F.I.R.M.A. Diagent (Florence, Italy) were used. Patch tests were applied on the upper back for 48h. Readings were performed 15-60 min after removal on days (D) 2, on D3 and on D7 in accordance with the recommendations of the European Society of Contact Dermatitis (ESCD) and the International Contact Dermatitis Research Group (ICDRG) [14, 15].

Statistical analysis

Unpaired Student's t-test was used to compare clinical data of male and female hairdressers. A *P* value ≤ 0.05 was considered significant.

Results

Gender distribution of OACD

In Italy in the period from 2014 to 2018 a total of 1555 patients with OACD were reported to INAIL, representing 63% of all reported occupational skin diseases, but less than 1% of the total number of reported diseases. There were 908 (58%) men and 647 (42%) women. The most common working sectors were industry and crafts in men, and services and public administration in women (Table 1). The causal agents most frequently involved were cement followed by epoxy resins in men, and hair dyes and rubber additives in women (Table 1). Most OACD were notified in Northern Italy. Of the individuals, 88% of workers were born in Italy, 3% in Albania and Romania, and 2% in North Africa. In Tuscany in the period from 2012 to 2019, 233 cases of OACD were reported to INAIL CPD Florence: 140 men (60%) and 93 (40%) women. The most commonly represented occupations were construction industry (24%), hairdressers (18%), healthcare sector (9%) followed by mechanical industry (7%) and food industry (7%) (Fig. 1).

Gender differences in hairdressers' OACD

In particular, 42 cases of OACD in hairdressers were reported to INAIL CPD Florence: 29 women (69%) and 13 men (31%). However, 23% of men and 24% of women had a positive history of family atopy; 31% of both genders had mucosal atopy, while cutaneous atopy prevailed in males (Table 2). Hand eczema was Table 1Gender-specific distribution of main workingsectors and causal agents in patients with occupationalallergic contact dermatitis (OACD). Italian National Institutefor Insurance against Accidents at Work (INAIL) nationaldatabase 2014–2018

	Men N (%)	Women N (%)
Working sectors		
Agriculture and fishing	14 (70)	6 (30)
Industry	273 (82)	59 (18)
Services	77 (25)	235 (75)
Crafts	144 (89)	17 (11)
Public administration	13 (20)	51 (80)
Not reported	387 (58)	279 (42)
Causal agents		
Chromate salts	30 (97)	1 (3)
Epoxy resins	44 (90)	5 (10)
Acrylic resins	6 (60)	4 (40)
Cement	58 (100)	0 (0)
Hair dyes	27 (26)	77 (74)
Rubber additives	19 (36)	34 (64)
Detergents	4 (19)	17 (81)
Cutting oils and fluids	29 (97)	1 (3)
Others	304 (57)	226 (43)
Not reported	387 (58)	282 (42)

a constant and the percentage of cases with diffusion to the forearms was similar in both genders, while generalized eczema with face involvement was more frequent in women who also suffered from occupational asthma (Table 2). In the cases observed, asthma was due to exposure to bleaching (ammonium persulfate), as evidenced by the positivity of the stop/ restart test. The onset of skin symptoms tended to occur later in men (39 ± 13 years) compared to women (34 ± 10 years), even if the men entered labor market earlier than the women (Table 3). The age at noti-



Table 2	Clinical	features	of I	hairdres	sers	with	occ	upa-
tional alle	rgic cont	tact dern	natit	is (OAC	D) re	porte	ed to	the
National I	nstitute f	or Insura	nce	against	Accie	dents	at V	Nork
(INAIL) Re	gional P	olydiagn	ostio	c Cente	r in F	lorer	ice,	Tus-
cany, Italy	(2012–2	019)						

	Women	Men	Total
Number of cases	29 (69%)	13 (31%)	42
ATOPY			
Family atopy	7 (24%)	3 (23%)	10
Personal skin atopy	1 (3%)	1 (8%)	2
Personal mucosal atopy	9 (31%)	4 (31%)	13
ECZEMA LOCATION			
Hands	29 (100%)	13 (100%)	42
Forearms	11 (38%)	4 (31%)	15
Generalized	6 (21%)	1 (8%)	7
ASTHMA	4 (14%) ^a	0	4

^a4 female hairdressers sensitized to ammonium persulfate

fication of the OACD to the workers compensation authority was lower in women (42 ± 15) than in men (50 ± 12) as well as the latency period, defined as the period from the beginning of occupational exposure to the onset of symptoms (Table 3).

Considering patch test results (Fig. 2), the most important contact allergens in hairdressers were hair dyes compounds (p-phenylendiamine, toluene-2,5-diamine, intermediates of their synthesis, stabilizers), followed by bleaches (ammonium persulfate and other oxidizing agents), nickel sulfate (released from metal tools), components of cosmetics (preservatives, biocides, perfumes), rubber additives (in particuTable 3Temporal occupational exposure of hairdresserswith occupational allergic contact dermatitis (OACD) reported to the National Institute for Insurance against Accidents at Work (INAIL) Regional Polydiagnostic Center inFlorence, Tuscany, Italy (2012–2019)

	Women mean±SD (min;max)	Men mean ± SD (min;max)	p-value
Age at the beginning of work (years)	18±2 (14;24)	17 ± 2 (14;20)	p<0.05
Age at onset of symptoms (years)	34±10 (19;56)	39±13 (18;61)	ns
Age at notification of OACD (years)	42±15 (21;67)	50 ± 12 (28;70)	ns
Latency period (years) ^a	16±11 (1:38)	22 ± 14 (1.5:46)	ns

^aDefined as the period from the beginning of occupational exposure to the onset of symptoms

ns not significant, SD standard deviation

lar, thiurams). Sensitization to p-phenylenediamine was higher in men (69%) than in women (59%), on the contrary sensitization to ammonium persulfate was more frequent in women (50%) than in men (30%). Sensitization to Disperse Orange 3 was equally distributed in both genders (40% in men vs 41% in women). Sensitization to methylchloroisothia-zolinone/methylisothiazolinone was higher in men (23%), while sensitization to fragrance mix I and rubber additives was found exclusively in women (Fig. 2). Positivity to *Dermatophagoides* mix was similar in male and female hairdressers (31% vs 28%). In addi-

Fig. 2 Patch test results in hairdressers with regard to the most frequently positive contact allergens selected from the Italian baseline, hairdressing and rubber additives series (in use at National Institute for Insurance against Accidents at Work (INAIL) Regional Polydiagnostic Center in Florence, Tuscany, Italy). All 42 hairdressers (13 men and 29 women) were tested with Italian baseline patch test series, 32 (10 men and 22 women) with the hairdressing series, 13 (4 men and 9 women) with the rubber additives series. MCI/MI methylchloroisothiazolinone/methylisothiazolinone



tion, subjects with sensitization to *Dermatophagoides* mix had history of atopy.

Discussion

Taken together all occupational diseases in Italy show a wide gender gap (73% in men vs 27% in women), while considering only OACD this gap narrows (58% in men vs 42% in women) [5, 6]. Gender distribution in OACD reflects differences in male and female tasks as evidenced by working sectors and haptens involved in the pathogenesis. As expected, women presented allergic contact dermatitis due to haptens found in their work environment (hairdressers, healthcare, beautician) and men presented allergic contact dermatitis due to haptens in their work environment (construction and mechanical industry).

However, when compared to other working sectors, male and female hairdressers are exposed to the same risk factors in the workplace (i.e., wet work and chemicals) as they generally perform the same type of work activities. For this reason, hairdressers represent an interesting model to analyze potential gender-related aspects in OACD. Both genders are exposed to the main phases of the hairdressers' activity, including washing, modification of hair color and hair shape, as well as stylistic works. Importantly, sensitization to p-phenylenediamine was confirmed to be the most frequent in hairdressers' OACD [16-19], and it was more commonly involved in men than women (Fig. 2). On the contrary, fragrance mix I and thiuram patch test positivity were found exclusively in women. Rubber additives sensitization could be correlated to the use of personal protective equipment and the higher proportion of women was probably due to the increased use of gloves among women that generally have a higher perception of risk compared to men [20]. Moreover, based on medical history, we found that there were no differences regarding atopy in male and female hairdressers affected by OACD. Hand eczema was a constant in both genders, while respiratory symptoms due to ammonium persulfate-a strong oxidizing agent in hair bleaches-were exclusively found in women. We observed that women tended to present and report OACD earlier than men, even if they entered the labor market slightly later than men. This anticipation in women could be related to a different social behavior of women compared to men. The latter might wait longer before notification of their disease to the compensation authority.

Despite the limited number of cases, this retrospective study has the advantage of investigating patients with OACD in whom the cause–effect relationship was recognized by the compensation authority (INAIL) and the clinical relevance of hapten sensitization was thoroughly established.

Conclusion

In hairdressers, hair color modification (dyeing and bleaching) represents the type of work associated with higher risk of causing OACD in both genders. Therefore, health surveillance, prevention, and educational interventions should be focused on this particular phase of hairdressers' activities [21, 22]. Clinicians should accurately record patients' occupation and consider the risk factors to which their patients are exposed according to their working tasks in order to define a tailored allorgologic work-up. A genderspecific approach to OACD and all other occupational diseases is essential to address the needs of female and male workers and orientate actions and policies, so that women and men benefit equally.

Compliance with ethical guidelines

Conflict of interest L. Salvati, E. Vanni, M.C. Acciai and P. Parronchi declare that they have no competing interests.

Ethical standards All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1975 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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