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On the behalf of the Italian Association of Hospital and Territorial Allergologists (AAITO - Campania district)

Sensitization to cockroach allergens in the urban atopic populations living in Campania district (southern Italy). A multicenter study

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KEY WORDS

Allergic rhinitis; allergic sensitization; bronchial asthma; Campania district; cockroach; cockroach allergy; hypersensitivity

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Summary

Background. Although cockroach (CR) is an important cause of allergic sensitization worldwide, only a few data are available in Italy and in a previous study we have observed, in Naples area, a low prevalence of CR sensitization. **Objectives.** We sought to perform a prospective study for assessing the prevalence of allergic sensitization to CR in a sample of atopic population living in Campania district area (Southern Italy). **Methods.** Ten Allergy Units or Centres of Campania district participated in this cross-sectional study. Each centre was required to collect the results of at least 100 allergy consultations in consecutive outpatients referred for actual or suspected respiratory allergy. We registered demographic data, type and duration of respiratory symptoms, pets ownership, possible exposure to CR allergens, results of the skin prick tests (SPTs). **Results.** A total of 1477 patients were examined, 985 (66.68%) had a SPTs positivity to at least one allergen. In this context, ninety were sensitized to CR, thus the overall sensitization prevalence in subjects with respiratory allergy was 6.09% ranging between 0-11% and only five patients were mono-sensitized. Thirteen patients reported rhinitis (R) + bronchial asthma (A), twenty-one R + A + conjunctivitis (C), thirty-seven R + C, five only A and eleven individuals only R. Sixty-seven patients exhibited persistent and twenty-three intermittent symptoms. Dust mite constituted the first cause of associated sensitization to CR. **Conclusions.** The prevalence of allergic sensitization to CR is not negligible in population living in Campania district and shows a higher trend in comparison to that found recently and some years ago in Naples area. Finally, we suggest atopic individuals and especially those highly sensitized to mite allergens or those living in low-income areas to be tested by SPTs / evaluation of serum specific IgE to CR allergens to exclude the occurrence of CR allergic sensitization.

Introduction

Although cockroach (CR) is an important cause of allergic sensitization worldwide (1, 2) only a few data are available in Italy. In adults, a mean 13% prevalence of allergic sensitization to CR has been shown in only one multicentre Italian study (3) while 4.58% and a peak of 20% have been found respectively in a study carried out in Naples area (4) and in another on the immigrants of Northern Italy (5). In children the prevalence is lower, ranging from 0.45 to 12.7% (6-8). It has been demonstrated that allergic sensitization to cockroach increases the risk of developing sensitization also to shrimp and house dust mite, because of the presence of IgE-binding cross-reactive epitopes between respective tropomyosins (9). Recently, we have shown that the prevalence of allergic sensitization to CR is still low (3.62%) in an atopic population living in urban area of Naples (10) and confirms the low trend found seventeen years ago (4.58%) (4).

However, since this low value does not necessarily reflect the true value of a larger territory such as the district area in which Naples is the chief town, we sought to perform a prospective study for assessing the prevalence of allergic sensitization, clinical characteristics and modality of exposure to CR in a sample of atopic population without occupational exposure living in Campania district area (Southern Italy).

Methods

Ten Allergy Units or Centres, uniformly distributed over the whole territory of Campania district (13.595 Km², 6.074.882 inhabitants) participated in this cross-sectional study. Each centre was required to collect the results of at least 100 allergy consultations in consecutive outpatients referred for actual or suspected respiratory allergy (asthma and/or rhinitis), starting from January 1 to June 30, 2011. 1477 subjects aged between 3 and 79 years (mean age 31.2) were examined.

All centres followed the same protocol. A case report form (CRF) containing all information and specifically designed for this study was completed during the screening consultation of each patient. The standardized form reported: demographic data, type and duration of respiratory symptoms, pets ownership, possible exposure to CR allergens assessed by some predictors (such as evidence of CR presence, poor housing conditions, etc.) (11), results of the skin prick tests (SPTs). The diagnosis of respiratory allergy was carried out according to the International Guidelines (12,13).

The commercial allergen extracts used for screening SPTs were provided by ALK-Abello Group, Milan, Italy. We used a standard panel of allergens including: *Dermatophagoides pteromyssinus* and *D. farinae*, *Alternaria alternata*, *Cladosporium herbarum*, cat and dog dander, *Parietaria*, grass mix, *Artemisia vulgaris*, *Olea europaea*, *Betula pendula*, *Cupressus sempervirens* and *Corylus avellana*. These allergens cover the majority of causative agents of respiratory

allergy in Italy. In addition we used allergenic extracts of cockroach (mix) provided by ALK-Abello Group, Milan, Italy. Positive (10 mg/ml histamine HCl) and negative (saline solution in glycerine-phenol solution) controls were used as well. SPTs were carried out and interpreted according to International Guidelines (14). The result was read after 15 minutes and expressed as the mean of the major wheal diameter plus its orthogonal. A 3 mm skin reaction or greater was considered positive. The profile of the wheals was outlined using a fine-point marking pen and transferred by adhesive tape onto patient's form.

Patients with chronic infectious diseases, malignancies or dys-metabolic diseases, severe cutaneous disorders, negative skin reaction to histamine, or in treatment with drugs interfering with skin response were excluded as well (15,16).

Results

A total of 1477 patients were examined. In this context 985 (66.68%) had a SPTs positivity to at least one allergen and were diagnosed as having respiratory allergy. The 1477 subjects had a mean age of 31.2 years (range 3-79) and 834 (56.46%) of them were females. 90 patients were sensitized to CR, 42 were females and 48 males. Thus, the overall sensitization prevalence in subjects with respiratory allergy was 6.09% ranging between 0-11% (**figure 1**). Only 5 patients were mono-sensitized to CR. 13 patients reported rhinitis (R) + bronchial asthma (A), 25 R + A + conjunctivitis (C), 36 R + C, 5 individuals only A and 11 only R. 67 patients exhibited persistent and 23 intermittent symptoms. 26 out of 90 patients reported some indoor conditions that constitute predictors for the presence of CR allergens. In 9 of these individuals we found the higher levels of cutaneous sensitization to CR, the remaining patients exhibited low/moderate degree of SPT positivity. Since the majority (85/90) of CR-sensitized patients showed cutaneous positivity to other common allergens (mites, pollens, moulds and pets) we could not quantify the role of CR sensitization in eliciting symptoms. The most common sensitizing allergens associated in CR allergic individuals are reported in **figure 2**. Dust mite constitutes the first cause of associated sensitization followed by *Parietaria*, grasses, *Artemisia vulgaris*, *Olea europaea* and pet danders. These findings are substantially similar to that found in Naples area in previous surveys (4,10). Since monoclonal antibody-based methods to measure the amount of CR allergens in the dust of indoor environments are not available in Italy, we have no information about the levels of indoor exposure to these allergens. However, Curtis-Brosnan et al. (11) have shown that patients' report on the presence of rodents at home and some predictors such as cockroach infestation and poor housing conditions may be sufficient to hypothesize CR allergen exposure in indoor environments. The main characteristics of the patients sensitized to CR are summarized in **table 1**.

Figure 1 - Geographic distribution of the Campania district centers with the percentages of subjects having positive skin reactions to cockroach allergens

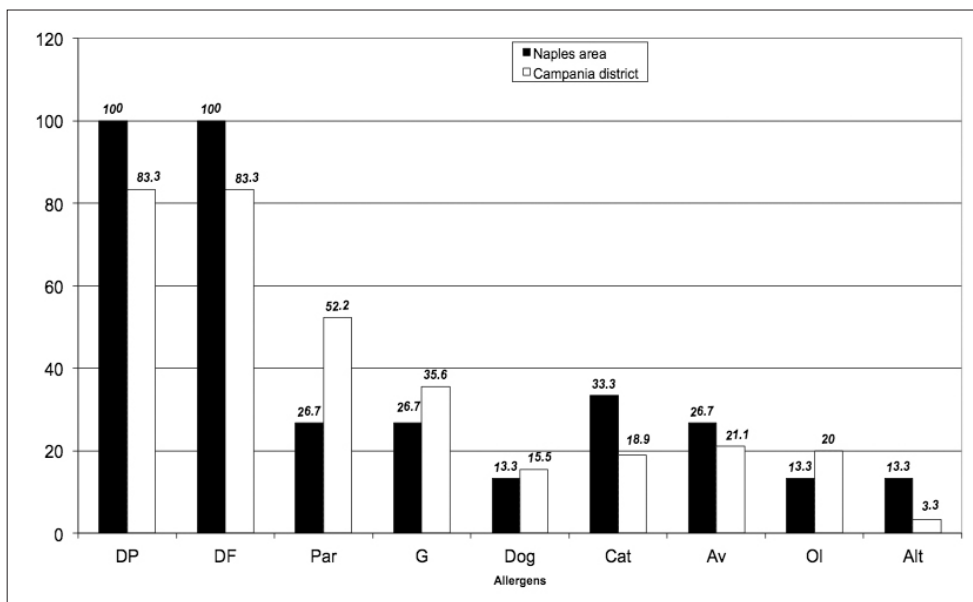
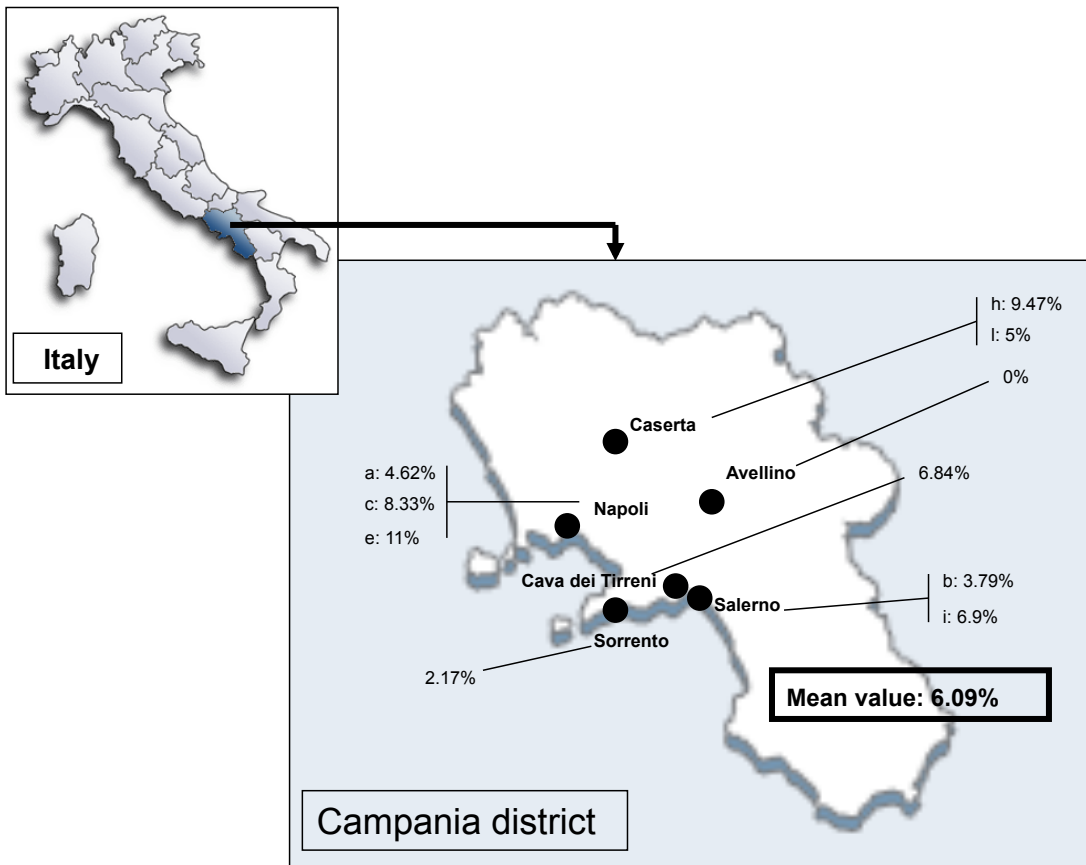


Figure 2 - Associated sensitizations

DP = *Dermatophagoides pteronyssinus*;
 DF = *Dermatophagoides farinae*;
 Par = *Parietaria*;
 G = Grasses;
 Av = *Artemisia vulgaris*;
 Ol = *Olea europaea*
 Alt = *Alternaria*

Table 1 - Characteristics of patients sensitized to cockroach allergens

	N°	Percentage
SEX (M/F)	42/48	46.7/53.3
MEAN AGE	45	
AGE RANGE		
- 0-20	25	27.8
- 21-41	46	51.1
- 41-60	14	15.5
- > 60	5	5.6
+ VE. FAMILY HISTORY OF ALLERGY	51 yes/39 no	56.7/43.3
PET AT HOME		
- Cat	6	6.7
- Dog	11	12.2
- None	70	77.8
- Other animals	2	2.2
- Cat + Dog	1	1.1
MODALITY OF EXPOSURE TO CR		
- Positive contact	26	28.9
- Negative contact	64	71.1
SMOKING		
- YES	12	13.3
- NO	70	77.8
- EX	8	8.9
CLINICAL SYMPTOMS		
-Rinithis (R) only	11	12.2
-Asthma (A) only	5	5.6
-Rinithis + Asthma	13	14.4
-Rinithis + Conjunctivitis (C)	36	40
-R + C + A	25	27.8
SEASONALITY OF SYMPTOMS		
- Intermittent	23	25.6
- Persistent	67	74.4
ASTHMA SEVERITY		
- Mild	20	22.2
- Moderate/Severe	70	77.8
MONOSENSITIZED TO CR	5	5.6
ASSOCIATED SENSITIZATIONS		
- Parietaria	47	52.2
- Dermatophagoides pteronyssinus	75	83.3
- Grasses	32	35.6
- Olive	18	20
- Mugwort	19	21.1
- Alternaria	3	3.3
- Cladosporium	1	1.1
- Birch	5	5.6
- Hazelnut	5	5.6
- Dog	14	15.5
- Cat	17	18.9
- Other allergens	8	8.9
DIAMETERS OF CR - ALLERGEN-INDUCED WHEELS (SPTs)	< 6x6 mm (81) > 6x6 mm (9)	90 10

Discussion

CR allergens constitute a common cause of allergic sensitization and bronchial asthma in children and adult populations of the US living in inner cities (1). CR exposure, independent of IgE-mediated sensitization status, constitutes also a relevant risk factor for asthma hospitalization in inner city children (17). Among several allergens produced by CR, it has been shown that sensitization to Per a 2 of the American cockroach correlates with more clinical severity among airway allergic patients (2). Wada et al. (18) have found that CR induces inflammatory responses through protease-dependent pathways. Additionally, genetic factors may play an important role in conferring the susceptibility to CR sensitization (19).

The results of this study suggest that the prevalence of allergic sensitization to CR allergens is not negligible in urban atopic population living in Campania district area. This rate of sensitization is higher in comparison to that found in Naples area in previous reports (respectively 4.58 and 3.62%) (4,10). In the three studies the main characteristics of CR-sensitized individuals (prevalence of female sex, high rate of family history of allergy, periods and type of clinical symptoms) may be easily explained by associated sensitization to other common allergens involved in all individuals. However, no specific symptoms related to exposure to CR were found in patients with higher degree of cutaneous sensitization to CR and also in five patients mono-sensitized to CR. The low prevalence of allergic sensitization to CR allergens in our previous study (10) is probably due to the rarely reported presence (only in two cases - 13.3%) of environmental conditions commonly considered at high risk for CR allergens presence (11). In the present study 26 (28.9%) patients reported ideal conditions for the presence of CR in indoor environments (11).

The associated sensitization to mite allergens in CR-sensitized individuals is a common feature in this as well as in the previous reports. Since CR and dust mites usually share the same indoor environments as well as some of their allergens, it is likely that these mechanisms could explain the finding of such a high prevalence of associated sensitization. Moreover, our study suggests that performing a multicenter study at level of district area is more likely to reflect the real rate of allergic sensitization to CR in Southern Italy in comparison to the rate of single urban area of Naples.

It is important to outline that the majority of patients referring to Allergy Services of Campania district who participated to this survey don't live in low-income areas of respective towns. This limitation is similar to that found in previous studies of Naples area. As a consequence, we cannot exclude that a survey carried out specifically in low-income areas of Naples and other towns of Campania district could reveal a higher prevalence of sensitization to CR.

In conclusion, the prevalence of allergic sensitization to CR is not negligible in population living in Campania district and shows a higher trend in comparison to that found recently and

some years ago in Naples area. Finally, we suggest that atopic individuals, especially those highly sensitized to mite allergens or those living in low-income areas, are tested by SPTs / evaluation of serum specific IgE to CR allergens to exclude the occurrence of CR allergic sensitization. We are planning further studies examining exclusively allergic individuals living in some low-income areas of Campania district to verify a possible increase in the rate of allergic sensitization to CR.

Authorship

All authors contributed equally to the writing and revision of the manuscript.

Conflict of interest and financial resources

All authors declare that they have no conflict of interest and that the study has been carried out without any financial support.

References

- Sohn MH, Kim KE. The cockroach and allergic diseases. *Allergy Asthma Immunol. Res* 2012;4:264-69.
- Lee MF, Song PP, Hwang GH, Lin SJ, Chen YH. Sensitization to Per a 2 of the American cockroach correlates with more clinical severity among airway allergic patients in Taiwan. *Ann Allergy Asthma Immunol.* 2012;108:243-48.
- Riario-Sforza GG, Della Torre F, Antonicelli L, Bonifazi F, Giordano T, D'Amato G, Liccardi G, Bettini P, Incorvaia C. Sensitization to cockroach in Italy, a multicentric study. *Allergy Asthma Proc* 1997;18:23-28.
- Liccardi G, Russo M, D'Amato M, Granata FP, De Napoli A, D'Amato G. Sensitization to cockroach allergens in a sample from the urban population living in Naples (Southern Italy). *J Investig Allergol Clin Immunol.* 1998;8:245-48.
- Lombardi C, Penagos M, Senna GE, Canonica GW, Passalacqua G. The clinical characteristics of respiratory allergy in immigrants in Northern Italy. *Int Arch Allergy Immunol.* 2008;147:231-34.
- Peruzzi M, De Luca M, Novembre E, De Martino M, Vierucci A. Incidence of cockroach allergy in atopic Italian children. *Ann Allergy Asthma Immunol.* 1999;83:167-71.
- Peroni DG, Alfonsi L, Ressa M, Milanese E, Piacentini GL, Boner AL. Low rate of cockroach sensitivity in Italian pre-school children. *Allergy.* 2002;58:531.
- La Grutta S, Cibella F, Passalacqua G, Cuttitta G, Liotta G, Ferlisi A, Viegi G. Association of *Blattella germanica* sensitization in pediatric allergic patients. *Pediatr Allergy Immunol.* 2011;22:521-27.
- Wang J, Calatroni A, Visness CM, Sampson HA. Correlation of specific IgE to shrimp with cockroach and dust mite exposure and sensitization in an inner-city population. *J Allergy Clin Immunol.* 2011;128:834-37.
- Liccardi G, Salzillo A, Piccolo A, Russo M, D'Amato M, Stanzola A, Bovenzi D, D'Amato G. Is sensitization to cockroach allergens changed during the last seventeen years in the urban atopic population living in Naples (southern Italy)? *J Investig Allergol Clin Immunol.* 2013;23:57-59.
- Curtin-Brosnan J, Matsui EC, Breyse P, McCornak MC, Hansel NN, Tonorezos ES, Eggleston P, Williams DC, Diette GB. Parent report of pests and pets and indoor allergen levels in inner-city homes. *Ann Allergy Asthma Immunol.* 2008;101:517-23.
- Bousquet J and The ARIA Workshop Group. Allergic rhinitis and its impact on asthma. *J Allergy Clin Immunol.* 2001;108:S147-S336.
- Global Initiative for Asthma. <http://ginasthma.org> (December 2012).
- Dreborg S, Frew A. Editors. Position Paper: allergen standardization and skin tests. *Allergy.* 1993;48 Suppl 14:49-82.
- Bousquet J, Michel FB. Precision of prick and puncture tests. *J Allergy Clin Immunol.* 1992;90:870-72.
- Wever AMJ, Wever-Hess J. Testing for inhalant allergy in asthma. *Clin Exp Allergy.* 1993;23:976-81.
- Rabito FA, Carlson J, Holt EW, Iqbal S, James MA. Cockroach exposure independent of sensitization status and associations for hospitalizations for asthma in inner-city children. *Ann Allergy Asthma Immunol.* 2011;106:103-09.
- Wada K, Matsuwaki Y, Moriyama H, Kita H. Cockroach indices inflammatory responses through protease-dependent pathways. *Int Arch Allergy Immunol.* 2011;155 Suppl 1:135-41.
- Gao P. Sensitization to cockroach allergen: immune regulation and genetic determinants. *Clin Dev Immunol.* 2012;2012:563760. Doi 10.1155/2012/563760. Epub 2012 Jan 9.