

Cypress pollen allergy in a Mediterranean area

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In recent years, an increase in the prevalence of *Cupressaceae-Taxodiaceae* pollen allergy in the Mediterranean area has been reported[1,2]. In order to assess its impact in our area, we carried out a prospective, cross-sectional study at Terrassa's Hospital, Vallés Occidental (Barcelona, Spain), an urban district with more than 800.000 inhabitants. The objectives of this study were: (1) to determine the annual incidence of pollen sensitization to *Cupressaceae* pollen in that population; (2) to describe its clinical characteristics and the molecular sensitization profile; (3) to test the diagnostic performance of pollen extracts for SPT, serum sIgE and NPT for the diagnosis of cypress allergy.

After signing the informed consent document, patients with symptoms suggestive of respiratory allergy and positive SPT to one or more of the three extracts of cypress pollen tested (*C sempervirens*, *C arizonica* and *Juniperus ashei*, Stallergens, France) were included in the study between February 1st 2010 and January 31st 2011. Demographic and clinical data were collected. Serum sIgE to the same 3 species (ImmunoCAP) and to molecular allergens (ImmunoCAP ISAC) was measured. NPT was performed with a *Juniperus ashei* (Stallergens, France) extract.

Symptom and medication use were recorded in a diary and cypress pollen concentrations were provided by the XAC. The gold standard were patients with *Cupressaceae* pollen positive SPT and concordant respiratory symptoms. Statistical analysis was performed using SAS 9.4 and SAS Enterprise 6.1.

A total of 1278 new patients were evaluated. Incidence of sensitization to *Cupressaceae* pollen by SPT was 15.1%, and decreased to 13.7% and 11% when considering positive sIgE to complete extract and individual allergens respectively.

The characteristics of *Cupressaceae*-pollen sensitized patients and the control group (sensitized to other aeroallergens) are shown in table 1, highlighting the statistically significant differences between both groups: (1) male gender was more frequent in the *Cupressaceae*-pollen sensitized children ($p = 0.04$); (2) a family history of atopy was significantly higher in children than in adults ($p < 0.0001$) in the control group; (3) sensitization to foods was significantly higher in the *Cupressaceae*-pollen sensitized patients ($p = 0.0005$), specially sensitization to peach (9/122, 7.3%), and (4) monosensitization was greater in the control group ($p < 0.0001$). *Cupressaceae*-pollen sensitized patients were predominantly residents in urban areas (88.5%) for an average of 22.1 years (range between 1 to 63 y).

Most patients were polysensitized (97.6%) and the most frequently detected concurrent sensitizations were to grass and olive pollen.

Wheals and sIgE values induced by *C arizonica* and *J ashei* were greater than those induced by *C sempervirens*.

Most of the patients were asymptomatic (72%) and rhino-conjunctivitis (16%) and rhinitis (9%) were the most frequent symptoms.

Molecular profiles of *Cupressaceae*-pollen sensitized patients showed: (1) sensitization to food cross-reactive allergens (LTP: 29%; seed storage proteins: 16%) and low sensitization to profilin (9%), thaumatin (7%) and polcalcin (2%) and (2) high percentage of sensitization to CCD-bearing proteins: Cup a 1: 91.4%; Cry j 1: 67%; Cyn d 1: 51%; Ole e 1*: 46.8%; Phl p 4: 30.8%; Pla a 2: 28.7%; Jug r 2: 11.7% and MUFX3: 6.3%.

The positivity to Ole e 1 ($p= 0.025$) and Jug r 2 ($p= 0.04$) were significantly associated to asymptomatic *Cupressaceae* sensitization.

A total of 71 specific NPT were carried out, 47 being positive (13 were allergic), 9 were negative and 15 were positive to saline serum (nasal hyperreactivity). NPT was highly sensitive (100%) but not very specific (15%) except for the concentration of 1 IR (69%).

In our study, the incidence of SPT sensitization to *Cupressaceae* and to the individual allergenic components were lower than those published of other geographical areas probably due to a greater presence of cypress trees in these geographic areas[3].

Sensitization to *Cupressaceae* pollen seems to develop at older ages than with other pollens and is always higher in adults (around 30 years[4]).

Peach sensitization in this study is similar to that described in patients sensitized to cypress pollen from southern France[5]. An important association between Cypress pollinosis, level of pollen exposure, and peach allergy due to peach pollen sensitization (Pru p 7) in French population, has recently been published. The authors describe that Cypress pollen extract completely outcompeted IgE binding to Pru p 7[6]. Monosensitization to cypress pollen was exceptional in our population, in accordance with previous studies[7].

All patients sensitized to nCry j 1 were also sensitized to nCup a 1, which is consistent with the high cross-reactivity described between both allergens[8]. The sensitization to polygalacturonase from plane tree pollen, nPla a 2, was higher than that described in the Central European population with pollinosis (15.5%)[9] and may be attributable to a genuine sensitization to *Platanus* pollen in a region with high exposure, as well as to

cross-reactivity either with *Cupressaceae* polygalacturonase or with CCD-bearing proteins.

In our study, sensitization to LTP was almost double to that detected among patients with pollen allergy (26,6% vs 12,3%)[10] but similar in patients with food allergy in Madrid (24% vs 37%)[10].

The lack of symptoms in our patients could be attributed to a diagnosis in a preclinical phase (patients complain of symptoms related to their sensitization to other pollens before symptoms related to *Cupressaceae* pollen develop) or to a true innocent sensitization.

The performance and interpretation of NPT were affected by: (1) the number of patients who underwent the NPT was small, and (2) the allergenic extract used (purified *J ashei*, predominantly monomeric) may not represent the native allergen and may induce a different clinical reactivity.

In summary, in the present study the incidence of sensitization to *Cupressaceae* pollen was 15%, despite most of the sensitized patients were asymptomatic and polysensitized. *C arizonica* pollen extract was the best to diagnose sensitization. Most patients were sensitized to nCup a 1, LTP and CCD-bearing proteins with a low prevalence of sensitization to profilins and polcalcins. NPT showed a high sensitivity with a low specificity, so it may help diagnose pollinosis to *Cupressaceae* in selected cases. Differences with other geographical regions raise the need for more local studies.

***In 2012 Ole e 1 was nOle e 1 in ISAC112®, nowadays is rOle e 1.**

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Conflict of interests

Dr. Castillo reports grant from Foundation of the Spanish Society of Clinical Allergy and Immunology (SEAIC), during the conduct of the study; and the allergenic extract used (purified J ashei standardized by Jun a 1) for the Nasal Provocation Tests were donated for free from Stallergenes S.A..

Dr. Olga Luengo has no conflict of interests to disclose.

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Table 1. Characteristics of *Cupressaceae*-pollen sensitized patients and control group.

		Cupressaceae-pollen sensitized (n=122) With symptoms n=26	Control group (n=530) With symptoms n=503
Age (years) Mean + SD	total adults children	31.1 (7-67) 36.3 (16-67) 11.2 (7-15)	27.3 (7-73) 34 (16-73) 10.8 (7-15)
Sex	female	adult	37.3% (198)
		children*	11.6% (64)
	male	adult	31.3% (166)
		children*	19.6% (102)
		56.5% (51) 26%* (18) p= 0.04	
Atopy	total adult children	44.2% (54) 40.6% (39) 42.3% (15)	45.2% (240) 42.3% (140) 70.7%*(100) p< 0.0001
Age at onset of symptoms, mean		22 year (1-66)	18.4 year
Symptoms	rhinitis	30.7% (8)	49.7% (250)
	rhinoconjunctivitis	57.6% (15)	13.7% (69)
	asthma	3.8% (1)	24.2% (122)
	rhinitis or rhinoconjunctivitis + asthma	3.8% (1)	11.5% (58)
	Rhinitis or rhinoconjunctivitis + spasmodic cough	3.8% (1)	0.79% (4)
Sensitization to foods		18%* (22)p=0.0005	7.3% (39)
Duration of allergic disease, median	Adults	7 year	ND
	Children	2 year	ND
Mono sensitization		2.4% (3)	36.4%* (193)p<0.0001
Total IgE, median		5.3	5.1

*statistical significance. ND: not done.