

***Alergológica* 2005. Methodological Aspects and Sample Characteristics of the Study**

F Caballero Martínez

Research Unit Coordinator Area 6 Primary Care, Madrid Health Service, Madrid, Spain

■ Abstract

Background: In this article we present the basic methodological aspects of the clinical epidemiologic study *Alergológica*-2005, a project launched by the Spanish Society of Allergology and Clinical Immunology replicating the objectives and methods of a similar study carried out in 1992.

Objective: The aim of this nation-wide study was to describe the profile of the patients treated in Spanish allergology departments, the normal clinical practice followed by the specialists in these departments, the social and healthcare repercussions of allergic diseases in Spain together with the additional objective of identifying any possible relevant changes that may have taken place regarding these factors during the decade since the original study was completed (1992-2005).

Methods: An observational, descriptive, cross-sectional study was carried out over the year 2005 using a convenience sample of allergic patients (recruited consecutively from a different random date for each researcher participating in the study) who were treated in the departments, both private and public, of 340 specialists in allergology working in the Spanish healthcare system. The sample was stratified geographically by autonomous region in a ratio proportional to the population of each geographical area.

Results: Clinical, epidemiological, diagnostic, therapeutic, social and general healthcare data were collected from 4991 allergic patients presenting for the first time in the departments of the researchers involved in the study. The results and conclusions will be presented classified by disorder in the following research articles published in this issue.

Conclusions: The methodological aspects described guarantee the accuracy of the estimates made in the current study and the comparability of the results with those of *Alergológica*- 92 project.

Key words: Allergy and immunology. Outpatient. Office visits. Morbidity. Physician's practice patterns.

■ Resumen

Antecedentes y justificación: Se presentan los aspectos metodológicos básicos del estudio clínico-epidemiológico *Alergológica* 2005, un proyecto impulsado por la Sociedad Española de Alergia e Inmunología Clínica replicando los objetivos y métodos de un estudio similar previo efectuado en 1992.

Objetivo: Se trata de un estudio de ámbito estatal que pretende describir el perfil de los pacientes atendidos en los Servicios de Alergología españoles, la práctica clínica habitual desarrollada por los especialistas de dichos servicios y la repercusión socio-sanitaria y asistencial de las enfermedades alérgicas en España, con la finalidad añadida de identificar las posibles modificaciones relevantes acaecidas en dichos aspectos durante la década transcurrida entre ambos estudios (1992-2005).

Métodos: Estudio observacional descriptivo de tipo transversal, realizado durante el año natural 2005, sobre una muestra de conveniencia de pacientes alérgicos (reclutada de forma consecutiva a partir de una fecha aleatoria personalizada para cada investigador de estudio) atendidos en las consultas de 340 especialistas en alergología, públicos o privados, del sistema sanitario español. La muestra se estratificó geográficamente por comunidades autónomas, en razón proporcional a la población de cada territorio.

Resultados: Se recopila información clínico-epidemiológica, diagnóstica, terapéutica, socio-sanitaria y asistencial de 4991 pacientes alérgicos (3.916 adultos y 917 niños) atendidos por vez primera en las consultas de los investigadores de estudio. Los resultados y conclusiones se presentarán, por patologías, en sucesivos artículos originales que se publicarán en esta misma fuente.

Conclusiones: Los aspectos metodológicos descritos avalan la precisión de las estimaciones del presente estudio y la comparabilidad de sus resultados con los del proyecto *Alergológica* - 1992.

Palabras clave: Alergia e inmunología. Paciente ambulatorio. Visitas a consulta médica. Morbilidad. Pautas de práctica clínica.

Background and Justification of the Study

In 1992, the Spanish Society of Allergology and Clinical Immunology (la Sociedad Española de Alergia e Inmunología Clínica (SEAIC)) launched and coordinated a clinical and epidemiologic project *Alergológica*, a nation-wide study which described the profile of the patients treated in a national sample of allergology departments and the normal clinical practice followed by the specialists in these departments [1].

After more than a decade of important scientific and technical advances and professional changes in Allergology in Spain, in 2005 the SEAIC re-launched a new edition of the study (*Alergológica-2005*) with similar objectives to those of the original project, and with the additional aim of identifying any possible relevant changes that may have taken place in the period between the two studies.

Several factors pointed to the possible importance of such changes in a specialty as relatively young as Allergology: the increase in the prevalence of allergic disorders and the healthcare demands thus generated [2-4]; evident allergenic changes in the environment [5,6]; the rapid social and demographic evolution of the Spanish population (due to migratory movements, among other causes) [7], the new technical and therapeutic advances recently incorporated into the specialty, the organizational changes brought about by the devolution to the autonomous regions of competences in healthcare, the generational turnover in the specialty, and so on.

The SEAIC hopes that the analysis of these changes will stimulate the identification of opportunities to improve healthcare provision in Allergology as well as the proposal of possible future lines of professional development and clinical research.

Specific Objectives of Alergológica-2005

- Describe the clinical and epidemiologic characteristics of the patients treated in the Allergology Services of Spanish health centers, and the prevalence of the different reasons for allergy-related consultations (rhinitis/conjunctivitis, bronchial asthma, urticaria/angioedema, atopic dermatitis, contact dermatitis, food allergies, drug allergies, hypersensitivity to hymenoptera, false allergies, etc.).
- Analyze any possible real differences in the regional distribution of allergic disorders in Spain, and the possible seasonal variability in the demand for allergy care in Spain.
- Describe the diagnostic procedure followed by the specialist and the actual use of diagnostic technology in allergology-related consultations.
- Describe the therapeutic procedure followed by the specialist, the real treatment guidelines used and the preventive measures instigated in allergology-related consultations.
- Calculate the social and health repercussions of allergic diseases on the quality of life of patients and on their educational and work activities.
- Describe the functional and organizational aspects

of consultations specialized in Allergology in the Spanish healthcare system in 2005 (the source of referral of patients, time on waiting lists, duration of the consultation, pressure on healthcare resources, and so on).

Methods

Design

This was an observational, descriptive, cross-sectional study with the prospective collection of data on patients treated for the first time in a wide sample of Allergology departments from all over the country.

Study Period

The field work was carried during the course of 2005, with two consecutive 4-monthly waves of patient enrollment (March – June and September – December). Both periods were chosen as they included expected peaks in the seasonal incidence of allergic disorders, which were the primary objectives of the research.

Subjects

The target population to which it was planned to extrapolate the overall results of the research were patients treated for the first time in public or private Allergology departments from all over Spain.

a) Inclusion criteria:

Patients of both sexes of any age. Patients treated for the first time for the current presenting complaint by the medical researcher: both new patients (never previously treated by the medical researcher) and patients already seen by the researcher who presented with a different complaint resulting from their previous allergy-related disorders were considered eligible. In both cases, the possibility of the patient having previously been treated by another allergologist was not an exclusion criterion in this study.

Patients who accepted to participate and for their clinical data to be used anonymously for the purposes of the study and who expressly gave their consent to the clinician responsible for data collection.

b) Exclusion criteria:

Patients currently participating (or who had participated in the previous trimester) in a clinical trial.

Patients with any physical or psychological impairment which might reduce or interfere with their understanding of the objectives of the study, their consent to participate or in the completion of the study surveys.

c) Sampling technique

Choice of researchers

All allergology specialists who were official members of the SEAIC and who were practicing clinically at the time of the study were voluntarily invited to participate. An initial

Table 1. Theoretical Sample Distribution Stratified Geographically by Autonomous Region and Real Data on Participating Researchers and Patients Recruited by the End of the Study Period

Autonomous Region	Population	% of Spanish population	Participating Allergologists	Patients Recruited	% Spanish Sample
Total	42.717.064	100.0%	340	4.991	100%
Andalucía	7.606.848	17.8%	61	886	17.7%
Aragón	1.230.090	2.9%	9	134	2.7%
Cantabria	549.690	1.3%	6	89	1.8%
C. La Mancha	1.815.781	4.3%	12	179	3.6%
Castilla y León	2.487.646	5.8%	21	311	6.2%
Cataluña	6.704.146	15.7%	54	786	15.7%
C. Valenciana	4.470.885	10.5%	36	537	10.7%
Extremadura	1.073.904	2.5%	9	134	2.7%
Galicia	2.751.094	6.4%	22	314	6.3%
Baleares	947.361	2.2%	8	119	2.4%
Canarias	1.894.868	4.4%	15	218	4.4%
La Rioja	287.390	0.7%	3	45	0.9%
Madrid	5.718.942	13.4%	42	611	12.3%
Navarra	578.210	1.4%	6	89	1.8%
País Vasco	2.112.204	4.9%	18	268	5.4%
Asturias	1.075.381	2.5%	9	134	2.7%
Murcia	1.269.230	3.0%	9	134	2.7%

forecast of an overall participation of 300 allergologists from all over the country was made. This group was then distributed by autonomous region in such a way that each regional subsample of researchers represented a similar proportion to that represented by the population of each region as determined by the latest national population census with the aim of reliably calculating the geographical distribution of these disorders in Spain and allowing comparisons between different regions to be made.

In those areas where the number of researchers available exceeded the needs of the study, a convenience sample was taken (after reaching agreement with the Scientific Committee of the study and the Governing Board of the SEAIC) with the criterion of distributing as widely as possible the geographical location of the researchers and representing the diversity of social and healthcare contexts which existed in each region. A regional coordinator, in representation of the Scientific Committee of the study, actively participated in the process of distribution and selection of researchers. Table shows the origin of the researchers stratified geographically and the recruitment of patients achieved by the end of the study period.

In order to also establish a professional subsample representative of pediatric allergologists which would allow the possible peculiarities in clinical practice of these subspecialists dealing exclusively with child allergies to be reliably evaluated, the stratified selection of a sufficient group of these professionals was planned taking into account their distribution over the whole country. Of the total number of registered pediatric allergologists who were members of the SEAIC at the beginning of the study (46 members) 26 finally participated.

• Patient selection

As no complete list of the study population (all allergic patients seen for the first time by the researchers throughout 2005) was available a priori on which to base the random or systematic recruitment of patients, a convenience sample was taken while at the same time attempting to control for the most obvious selection biases involved in this process.

Thus, researchers were assigned a personal random date from which they could begin the inclusion of eligible patients from their consultations until the personal quota of 15 cases had been reached. From the established date, each researcher recruited the first patient attended on the day who was eligible and gave consent. In this way, in each working day the researcher could recruit a maximum of 2 patients until the sample requirements were met. The dates for beginning patient recruitment for each researcher were distributed homogeneously over each 4-monthly wave of the study.

In order to represent the proportion between public and private consultations existing in Spanish allergology services and to identify the possible differences in clinical practice determined by each context, researchers with a mixed practice distributed the 15 cases in the same proportion as was represented by private and public patients in their daily work. For this, each clinician based this calculation on the number of public and private patients seen in the week prior to the beginning of the study.

In those cases where it was impossible for patients to be included in the dates or order as initially planned, a special system was used whereby in the case of failure the immediately consecutive patient or day was used as a substitute.

c) Sample size

The Scientific Committee extended the original number of participating researchers to 340 to guarantee the appropriate representation of all the different healthcare contexts in each region.

This group of researchers finally obtained a national sample of 4991 patients, a number that ensures a high level of accuracy in the general estimations of the study even when the data are subcategorized and analyzed at the local level. Even in the most mathematically unfavorable of conditions (response rate in the variables with binomial distribution $p=q=0.5$), supposing a random sample and for a confidence level of 95%, the national results could be calculated to an accuracy of + 1.4%.

The overall sample is composed of 3916 adult patients and 917 children (≤ 14 years of age). Of the child subsample, 394 patients came from exclusively pediatric allergology consultations.

Measurements and study variables

The study protocol was adapted from that used in the first *Alergológica* study (in 1992) [1] so as to allow comparison with the main data obtained then and detection of any relevant changes in the prevalence and clinical manifestations of the disorders, the demand for patient care and the clinical practice of the clinicians.

Minor changes were incorporated due to the diagnostic or therapeutic advances made in the period between the studies, or methodological improvements over the first study currently available (for example, the use of the Spanish version of SF-12 [8, 9] as a validated questionnaire to reliably measure the quality of life of the allergic patient).

Data collection and instrumentalization of the study

a) Completion of the data collection record (DCR):

Each researcher was informed by a regional supervisor of all the methodological aspects of the project, of the specifications of the field work and the contents of the data collection record designed for the study. To this end, a researcher training strategy was planned which allowed personalized training meetings for each researcher to be held, in small groups and near the researcher's normal home.

In order to guarantee the involvement and permanence of the researchers in the project, before the period of inclusion of patients began and during the time that this lasted, participating clinicians received either by e-mail or telephone messages reminding them of the appropriate dates for recording information.

Researchers attempted to complete the full record of information laid out in the study protocol by filling in a printed paper copy of the DCR for each patient in the study, as far as possible during the recruitment consultation. If the time available or particular study needs (waiting for the results of complementary tests, etc.) forced the completion of the record to be delayed, researchers were asked to complete the DCR as soon as possible during subsequent patient visits. Loss of participants due to patients not attending subsequent consultations was resolved by substituting the lost patient by the first new available patient to be seen after the missed appointment.

b) Follow-up and monitoring of the field work

The DCR sheets from *Alergológica*-2005 were edited in duplicate with self-copying paper so that the researcher and the supervisor could each have a copy of the records. The completed DCRs were sent by post to the Monitoring Office which was responsible for the management of the study and ensured the quality of the information collected by reviewing missing, erroneous or inconsistent data. When necessary, researchers and supervisors were informed by fax or e-mail of the information to be corrected or recovered. Within established time limits, each investigator had to return the instruction in writing and appropriately validated (with a signature).

Using their own criteria, the regional supervisors established the necessary personal contacts with the participating researchers to maintain motivation and guarantee the completion of the study. If geographical proximity allowed and the deficiencies noted warranted it, these supervisory tasks were carried out in person.

Statistical analysis

The prevalence in the study consultations of the different allergic disorders was calculated and the remaining qualitative variables of interest were described by calculating relative frequencies (%) and the 95% confidence interval. Quantitative variables were described using commonly used measures of centrality and dispersion (mean and standard deviation), and the median and other frequently used rank indicators (quartiles, interquartile range and adjacent values) when the data were widely or atypically dispersed.

The percentage differences in the distribution of qualitative variables was compared by determining the 95% confidence interval of the difference between percentages and/or using the Chi-square test (or Fisher Exact test) as appropriate. The comparison of average values in quantitative variables was made using the Student t test (or the Mann-Whitney U test, if the characteristics of the subsamples required it) or the analysis of variance (or the Kruskal-Wallis test) in cases of multiple comparisons, complemented by an a priori test of multiple comparison (Bonferroni, Tukey).

The quality of life related to health data, quantified by the SF-12 questionnaire were measured using specific software which allowed each patient's scores on the two subscales of the questionnaire (the mental subscale or MCS-12 or the physical subscale or PCS-12) to be extracted. Sample averages of these subscales with the distribution in percentiles of the average scores for the general Spanish population were compared.

All data were analyzed using the statistical package SPSS-W (version 14.0).

Ethical considerations

Alergológica-2005 is a descriptive cross-sectional study favoring a naturalistic approach in which the conditions of normal clinical practice were maintained at all times, without any additional interventions on the patients other than those deemed opportune by the clinician in the management of the disorder in question.

Although the patients recruited ran no additional risk by participating in the study which was organized following the international norms relative to the undertaking of epidemiologic studies as described in the International Guidelines for Ethical Review of Epidemiological Studies (Council for the International Organizations of Medical Sciences-CIOMS-Ginebra, 1991) and the recommendations of the Spanish Society of Epidemiology (Sociedad Española de Epidemiología (SEE)) in their review of the ethical aspects of epidemiologic research, the study was submitted for evaluation and was approved by the Clinical Research Ethics Committee of the Hospital Central de la Defensa, Madrid.

Eligible patients were informed by their doctors verbally and in writing, with the help of an information sheet describing the objectives of the study, the methodology, the problems, risks and possible benefits of participation as well as the full confidentiality of the clinical data collected. After this, express consent was asked for by the patient signing the printed document. In under age patients or those incapable of providing consent, agreement to participate was obtained from at least one of the parents or the legal guardian.

As far as the data from the study are concerned, in accordance with the stipulated by The Organic Law 15/1999 of 13 December concerning "the Protection of Personal Data", no information was recorded relative to the identity of the patients in the DCR. Furthermore, all clinical information was reported anonymously and independently of personal details being linked to a code (the patient number) only known by the researcher responsible for each patient. The definitive database generated for the study contained no identification of the patients which could allow their identities to be revealed.

Results and conclusions

The Alergológica-2005 study described in the present article has collected clinical, epidemiologic, diagnostic, therapeutic, social and healthcare information from 4991 allergic patients (3916 adults and 917 children) treated for the first time in the departments of the study researchers. The results and conclusions will be presented categorized by disorder in the following articles in this issue.

The methodology of the study, appropriately updated and optimized, replicates that of Alergológica-1992. The study size achieved, the technical precautions regarding the nation-wide distribution of participants and the control of selection biases, the unification of the scientific and technical criteria among the researchers responsible for the field work, and the tasks planned for the monitoring, supervision and quality control of the information collected guarantee both the accuracy of the results of the present study and its comparability with the Alergológica-1992 project.

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■ Fernando Caballero Martínez

Zurbano, 56 - 1°C, 28010 Madrid
Tel.: (+34) 91 602 69 43 – Fax: (+34) 91 639 45 01
E-mail: fcaballero@papps.org