Epidemiology, healthcare, resources, use and clinical features of different types of urticaria. *Alergológica 2005*

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Abstract

Introduction: In spite of the impact on quality of life, little attention has been given to chronic urticaria.
Objective: To describe the morbidity and features of urticaria and compare the results with the other allergic diseases included in this study.
Results: Urticaria is the fourth most prevalent condition after rhinitis, asthma and drug allergy. Despite this position, the number of patients who needed to visit emergency departments was higher (54.4%) than the rest of the sample (24.6%) ($P<.001$). The percentage of urticaria/angioedema patients with work absences was also higher than the rest of the sample suffering from other allergic conditions. We found significant differences in school performance between urticaria/angioedema children and children from of the rest of the sample ($P=.029$). Paired analysis identified significant differences in percentages of "bad school performance" for children suffering from urticaria/angioedema. Patients suffering from chronic urticaria scored in the lowest 25th percentile on physical impact. On psychological impact, urticaria patients scored below the 20th percentile of the general population. The general trend was to order extensive laboratory test for patients suffering from urticaria. In the present study, only one patient had a systemic disease, 13 patients had autoimmune and endocrine diseases often present with chronic urticaria. In spite of the insistence on the possible role of infections in chronic urticaria, in our study an infection could only be demonstrated in three patients.
Conclusion: Based on these results, we believe that urticaria is a disease with significant morbidity and involves heavy use of healthcare services and as such deserves more resources and attention.

Key words: : Acute urticaria. Physical urticarias. Chronic urticaria. Epidemiology. Quality of life.

Resumen

Introducción: A pesar del impacto sobre la calidad de vida que supone la urticaria, se le dedica poca atención.
Objetivos: Describir las características de la urticaria y compararlas con las halladas en el resto de patologías alérgicas.
Resultados: Es la cuarta causa de consulta al alergólogo por detrás de rinitis, asma y alergia a medicamentos. A pesar de ocupar la cuarta posición, el porcentaje de pacientes con urticaria (54,4%) que han consultado en urgencias es más del doble que el de la muestra general (24,6%) ($P<0,001$).
El porcentaje de pacientes con urticaria/angioedema que han precisado baja laboral en el último año por su problema alérgico es superior al de la muestra general. Existen asimismo diferencias en el rendimiento escolar con el resto de pacientes alérgicos ($P=0,029$). Con respecto a la calidad de vida, en la subescala de puntuación de calidad de vida "física" el promedio de los pacientes con urticaria/angioedema se sitúa en el percentil 25 de la distribución de puntuaciones de calidad de vida y el promedio de calidad de vida "psíquica" por debajo del percentil 20. La tendencia diagnóstica es realizarles a los pacientes con urticaria múltiples tests. En el caso de urticaria crónica hallando únicamente en un caso una enfermedad sistémica, 13 patologías endocrinológicas autoinmunes que suelen coexistir con urticaria y sólo se pudo detectar infección en un caso.
Conclusión: teniendo en cuenta nuestros resultados pensamos que la urticaria es una enfermedad con alta morbilidad, y que supone un gasto sanitario importante.

Palabras clave: Urticaria aguda. Urticarias físicas. Urticaria crónica. Epidemiología. Calidad de vida.

Introduction

Among the disorders included in the present study, urticaria is the disease that had the highest impact on quality of life and required most visits to the Emergency Department. Moreover, urticaria was the disease with the strongest impact on school performance and caused the highest number of absences from work due to sickness.

Material and methods

The study on urticaria was part of a nationwide cross-sectional study. Data were collected through a questionnaire completed by allergy specialists. For quantitative variables, we utilized student t test or U Mann-Whitney test as required. For multiple variables, we employed the Kruskal-Wallis test with Bonferroni or Tukey correction.

Prevalence

539 (10.8%) of the patients included in the present study were diagnosed with urticaria with or without angioedema. It was the fourth most important allergic condition after rhinitis, asthma and drug allergy. This position was the same as in the 1992 study. These data agree with a large population study [1] performed in our country.

Demographics

The mean age of urticaria/angioedema patients was 35.75 ± 18.9 years with a maximum incidence at 49 years. The percentage of pediatric patients was only 13.4%. We found a significantly higher prevalence (62.8%) of urticaria/angioedema in women.

We did not observe any significant differences depending upon rural or urban residence, household, education level, race, occupation, income or having pets at home.

Utilization of healthcare services

Three hundred ninety two patients reported having sought medical care over the previous year. 72.3% of patients went to their family doctor an average of 2.33 ± 2 times. Two hundred thirty-three patients went to the Emergency Department. Interestingly, we found significant differences in the number of patients who needed to visit emergency departments between urticaria/angioedema (54.4%) and the rest of the sample (24.6%) ($P < .001$). Moreover, this percentage has increased from the 1992 study (49%). The number of emergency visits was also higher in urticaria/angioedema patients (1.8 times/year) than the rest of the sample (1.76 times/year) with no significant differences.

However, only fourteen patients had a urticaria/angioedema-related hospitalization with an average stay of 2.6 ± 2 days and a maximum stay of 7 days.

When analyzing the type of healthcare utilized, 81.5% were treated by public health services, 13.3% made outpatient visits covered by private health companies and 5.2% were seen in outpatient private practices paid for by patients. In the 1992 study we found 9.7% of urticaria patients in private practice that are now absorbed by private health companies.

More than half of the patients (55.4%) visiting an allergist were referred by primary care physicians, whereas 28.1% were referred by other specialists. The specialists who asked for a referral to an allergist were dermatologists, emergency doctors and pediatricians.

When we analyzed the delay in the public system to be seen by an allergist for urticaria/angioedema, we found an average of 82.48 ± 123.5 days with a maximum delay of two years. When percentiles were analyzed the highest distribution corresponded to 7 months.

When the delay to be attended by an allergist was compared with the overall data (76.89 days), the average overlapping confidence intervals (76.9 95% CI, 73.19-80.59 vs. 82.5, CI, 82.48, 0-900), showed no significant differences between urticaria/angioedema patients and the rest of patients suffering from other allergic diseases ($P = .35$).

Absences from work

Of the 392 patients who needed medical attention, 34 required an absence from work in the previous year with an average of 1.52 ± 0.87 work absences per year. The average absence from work was 15.52 ± 22.56 days.

Again, the percentage of urticaria/angioedema (7.7%) patients with work absences was higher than the rest of the sample (5.1%) with other allergic conditions ($P = .017$).

Absences from school

When children were studied, 7.4% of patients missed school because of urticaria/angioedema with an average of 7.5 ± 18.5 missed days. Interestingly, 3.3% of children with urticaria also caused their parents to take days off work.

School performance

We found significant differences in school performance between urticaria/angioedema children and children from the rest of the sample ($P = 0.029$). Paired analysis identified significant differences in percentages of "bad school performance" for children suffering from urticaria/angioedema (4.8% were classified as having bad school performance in the chronic urticaria group vs. 1.9% en the general sample). As for the duration of absences from school, 19.5% of children were absent for one day, 19.55% for two days, 17% for three days and 12.2% for five days because the urticaria.

Quality of life

Chronic urticaria had a significant impact on quality of life. Patients suffering from chronic urticaria scored in the lowest 25 percentiles on physical impact in the SF-12 Quality of Life questionnaire. When analyzing the psychological impact, urticaria patients scored below the 20th percentile as compared with the general population.

Urticaria/angioedema patients gave the worst score on the mental section of the SF-12 questionnaire and scored in the fifth

Table 1. Identified Causes of Acute Urticaria

		Number of Cases	% of Total
Foods		56	19.7%
Drug		27	9.5%
Parasites		23	8.1%
	Anisakis	20	8%
	Hydatidosis	0	0%
	Ascaris	2	0.7%
	Lamblia	1	0.4%
Physical urticaria		15	5.3%
	Dermatographism	9	3.2%
	Cold	3	1.1%
	Contact heat	2	0.7%
	Solar	1	0.4%
	Exercise	3	1.1%
Syndromes that can be associated with urticaria		12	4.2%
Insect bites		6	2.1%
Additives		2	0.7%

Table 2. Tests Performed on Patients with Acute Urticaria

		Number of Cases	% of Total
Clinical history and physical examination		249	87.7
Skin tests to foods		168	59.2
Skin test to inhalants		159	56.0
IgE			
	Total	142	50.0
	Specific	47	16.5
Blood count		139	48.9
Biochemistry		134	47.2
Erytrocyte sedimentation rate		122	43.0
Immunologic tests		95	33.5
	ANA	68	23.9
	Anti-thyroid antibodies	47	16.5
	Rheumatoid factor	46	16.2
	Immunoglobulins	59	20.8
	Complement	84	29.6
		67	23.6
Thyroid function		64	22.5
Stool parasites		52	18.3
Serologies		42	14.8
X Ray		38	13.4
Physical urticaria tests		31	10.9
Patch tests		17	6.0
Helicobacter pylori test		14	4.9
Autologous skin test		1	0.4

place in the physical section of the questionnaire when compared to all allergic conditions included in the present study.

Clinical features depending on urticaria type

We will now distinguish the clinical features depending on the type of urticaria. Based on the European Academy of Allergology and Clinical Immunology classification of urticaria [2], 53.4% of patients visited the allergist because of acute urticaria and 46.6% because of some other type of chronic urticaria. 12.3% of patients suffered from isolated angioedema and 30.8% urticaria accompanied by angioedema. For the present study we followed recent urticaria classifications, taking in account that two urticaria types could coexist in one given patient.

Acute urticaria

Identified causes

We include in Table 1 identified causes found for acute urticaria. As can be seen, the most frequent was food allergy. Parasites reached such a high number (8.8%) as Anisakis was included as a parasite.

An infection was demonstrated in only eleven patients without any other pathological findings.

Tests performed

We summarize in Table 2 the tests performed on patients with acute urticaria. In 69.4% of the cases, skin tests were performed, and in 56% of patients a blood test was done. Furthermore, in 33.5% of cases, an immunologic test was carried out. Complement was studied when angioedema was the case.

Chronic urticaria

Identified causes

Table 3 summarizes the identified causes of chronic urticaria. These data agree with previous studies that established that only in between 20% and 25% of chronic urticaria patients could a cause be found [3]. In our study, physical urticarias were found in 20.5% of patients including cholinergic urticaria. In 4.8% of cases, food allergy was implicated.

In spite of extensive studies, no cause was found in 75% of chronic urticaria patients and these cases were thus classified as idiopathic.

Anisakis sensitization was found in fewer patients in the chronic urticaria group than in the acute urticaria group.

Despite the attention given to additives and preservatives as a possible cause of chronic urticaria, in only one patient with chronic urticaria were additives involved and no specific tests to identify the culprit additive were performed.

Table 3. Identified Causes of Chronic Urticaria

		Number of Cases	% of Total
Physical urticaria		39	15.7
	Dermatographism	24	9.7
	Cold	11	4.4
	Exercise	5	2.0
	Pressure	4	1.6
	Heat contact	4	1.6
	Aquagenic	2	0.8
	Solar	1	0.4
	Vibratory	0	0
Parasites		13	5.2
	Anisakis	8	3.2
	Hydatidosis	0	0
	Ascaridiasis	1	0.4
	Lambliasis	1	0.4
	Other	3	1.2
Cholinergic urticaria		12	4.8
Food allergy		12	4.8
Drug allergy		2	0.8
Insect bites		1	0.4
Hereditary angioedema		1	0.4
Additives		1	0.4
	Conchinchilla red	0	0
	Tartrazine	0	0
	Sulfites	0	0
	Glutamate	0	0
	Other	2	0.8

Associated diseases

Five patients suffered from an autoimmune disease, two from connective tissue disease, seven patients had different endocrine conditions and one patient had a myeloproliferative disease.

It is worth commenting that these data confirm the known association of chronic with other autoimmune conditions such as autoimmune thyroiditis [4].

In spite of the insistence on the role of infections in chronic urticaria, in our study an infection could only be demonstrated in three patients.

Tests performed

We summarized all tests performed on chronic urticaria patients in Table 4. Thyroid functional test were performed in 62.1% of chronic urticaria patients and autologous skin tests in 1.2% (11). It took 26.14 ± 27.12 days to reach the diagnosis of chronic urticaria.

Family history

We found a significantly lower risk of family history for asthma and rhinitis ($P < 0.001$) when compared with the rest of the sample.

Table 4. Tests Performed on Patients Suffering From Chronic Urticaria

		Number of Cases	% of Total
Clinical history and examination		230	92.7
Blood count		191	77.0
Biochemistry		186	75.0
Erythrocyte sedimentation rate		177	71.4
Food skin test		174	70.2
IgE			
	Total	167	67.3
	Specific	112	45.2
Immunology test		168	67.7
	ANA	132	53.2
	Complement	150	60.5
	Thyroid antibodies	112	45.2
	Immunoglobulins	105	42.3
	Rheumatic factor	75	30.2
Inhalants skin tests		155	62.5
Thyroid function test		154	62.1
Protein S		119	48.0
Stool parasites		96	38.7
Serologies		78	31.5
Physical urticaria tests		55	22.2
X-Ray		44	17.7
Helicobacter pylori		36	14.5
Patch skin test		17	6.9
Autologous skin tests		3	12
Skin biopsy		2	0.8
Additives tests		0	0

Table 5. Types of Physical Urticarias

Type of Urticaria	n	%
Dermatographism	24	9.7
Cold urticaria	11	4.4
Exercise	5	2.0
Pressure	4	1.6
Heat	4	1.6
Aquagenic	2	0.8
Solar	1	0.4
Vibratory	0	0

Personal history

We also found a significantly lower risk of personal history for asthma and rhinitis when compared with the general sample ($P < .001$).

Physical urticarias

Data are included in Table 5. Dermatographism and cholinergic urticaria were the most frequent physical urticarias found, followed by cold and pressure urticaria. The rest of physical urticarias were hardly ever found.

Hereditary Angioedema

Two patients were diagnosed with hereditary angioedema (HAE). The disease has a prevalence of 1.09 per 100,000 habitants in Spain [1]. Our data corresponded to the number of patients visiting an allergist so they did not indicate prevalence for the general population.

Treatment

From the total 539 patients included in this study, 469 were receiving pharmacological treatment. 73.3% received antihistamines as recommended by the guidelines [5-7]. Regarding the type of antihistamine utilized, 12% of patients used first generation sedating antihistamines, 74.4% non-sedating antihistamines. 9.1% of patient needed to employ systemic corticosteroids.

Antifibrinolytic agents and C1 inhibitor correspond to the treatment indicated to patients suffering from HAE.

Discussion

As was recently described by one of the leaders in this field, chronic urticaria is a 'Cinderella disease' [8] with a high impact on quality of life and health care costs [9]. Moreover, we demonstrate in the present study that urticaria/angioedema is a disease with significant morbidity that should be taken in account.

Our study supports this observation when we compare urticaria/angioedema with other allergic conditions. Thus, despite the high attention given to asthma and rhinitis, our data show that among other allergic conditions, the percentage of patients with urticaria who visited emergency departments because of their urticaria/angioedema was double the percentage of patients that visited emergency departments because other allergic conditions. Moreover, this percentage has increased from the 1992 study. The number of emergency visits was also higher in urticaria/angioedema patients than the general sample. Moreover, the percentage of urticaria/angioedema patients with work absences was also higher than the rest of the sample suffering from other allergic conditions. Thus, urticaria deserves more resources and attention and the number of papers and teams dedicated to this field given the morbidity this disease leads to, is surprisingly low.

The impact on quality of life was also highlighted in our study. When compared with other allergic conditions, urticaria was the disease with the greatest impact on mental performance. These data closely agree with previously published data [10-12].

Furthermore, we found other factors that could negatively contribute to quality of life of chronic urticaria patients, such as the number of tests performed. This is not consistent with what has been recommended in several recent guidelines [5-7]. Such a wide range of tests had very low diagnostic efficiency and no cause was found in seventy five percent of the patients.

A careful history and examination remains the best diagnostic tool. A systematic review [13, 14] advises against an extensive test panel suggesting blood count, erythrocyte sedimentation rate and a urine test and performing extensive tests only when suggested by the history. In addition, ordering such a wide number of tests also dramatically increases healthcare costs with no benefit to the patient [15].

In contrast, the diagnostic performance for physical urticaria tests was very high. When the percentage of tests performed was compared with the diagnosis reached, we found 75% of tests to be positive in Dermatographism, 73.3% in cold urticaria and 100% in cholinergic urticaria. This was not the case with pressure urticaria that could be only demonstrated in four of the 14 patients in whom tests were performed. In spite of this good performance, it is remarkable how in only 22.2% of patients with chronic urticaria physical tests were performed. This could be due to the lack of standardization for such tests.

Regarding treatment options, a high percentage of patients are still treated with sedating antihistamines that could also negatively influence the quality of life of patients with chronic urticaria.

As has been previously reported by several studies, [16-18], we also found a significantly higher prevalence of urticaria/angioedema in women. The cause of this difference between sexes is not known. It might be due to the autoimmune mechanism of chronic urticaria and as it is well known that autoimmune diseases are more frequent in women. However, we observed an increase of 29.5% in the prevalence in men when comparing the present study with that performed in 1992. It is also interesting to note that when sexes were compared in children no differences were observed.

The negative family and personal histories for allergies strongly point to the fact that in the case of chronic and physical urticaria an allergic condition is not the cause. It would be very interesting to perform more studies differentiating between family and personal history depending upon urticaria type.

Our data showed that currently the approach to a patient suffering from urticaria/angioedema is to look for an underlying disease as a cause should be found. In the meantime, we must convince both clinicians and patients that following guidelines, standardizing tests for physical urticarias, and dedicating resources and time to basic research will benefit patients, make huge economic savings and set the ground for carrying out well designed research studies.

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