

Title: Real-Life Approach and Treatment of Chronic Urticaria in Argentina: A National Survey

Authors: Torre Ana Clara, MD^{1, 2}, Bollea Garlatti Maria Luz, MD¹, Marciano Sebastián, MD, MsC³, Posadas-Martinez María Lourdes, MD, MsC, PhD³, Parisi Claudio Alberto Salvador, MD^{2, 4}, Mazzuoccolo Luis Daniel, MD, MPH¹.

¹ Department of Dermatology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

² UCARE center, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

³ Department of Research, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

⁴ Department of Internal Medicine, Allergy Section, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Corresponding author:

Ana Clara Torre, MD

Department of Dermatology, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina.

Address: Perón 4230, Buenos Aires, Argentina

E-mail: anaclaratorre@gmail.com

Keywords: Guidelines, Therapeutics, Urticaria, Survey

Running short title: Approach and Treatment of Chronic Urticaria: Survey in Argentina

Conflicts of interest disclosure:

- Ana Clara Torre: Honoraria for lectures and research work from Novartis
- Maria Luz Bollea Garlatti: No conflict of interest to declare
- Sebastian Marciano: No conflict of interest to declare
- Maria Lourdes Posadas: No conflict of interest to declare

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/dth.13086

- Claudio Alberto Salvador Parisi: Honoraria for lectures from Novartis
- Luis Daniel Mazzuoccolo: Grant and Lectures from Novartis

Abstract

Background

The management of chronic urticaria (CU) has been controversial. Recently updated international guidelines propose evidence-based diagnosis and treatment. Nevertheless, dermatologists have heterogeneous approaches to managing CU.

Purpose

To estimate the percentage of dermatologists who have an optimal approach to CU according to the international guidelines, and to explore the variables associated with optimal management.

Method

A cross-sectional study using a 17-question survey was delivered by email to dermatologists from Argentina. Optimal first, second and third line treatment were considered when dermatologists chose a non-sedative antihistamine; increased the dosage of non-sedative antihistamines, and added omalizumab, respectively. Logistic regression was used to identify variables associated with optimal management.

Results

A total of 165 questionnaires were available for analysis. An optimal first, second, and third-line treatment approach was identified in 50%, 35%, and 15% of the dermatologists, respectively. The dermatologists' age being above 55 years old (OR: 0.12, 95% CI: 0.01-0.99, p 0.005) and having more than five years of expertise (OR: 0.4, 95% CI: 0.19-0.81, p 0.001) were significantly associated with a suboptimal approach in second-line treatment. We could not find variables associated with an optimal first or third-line treatment.

Conclusion

The real-life management of CU in Argentina is partly suboptimal according to the international guidelines.

Keywords: Guidelines, Therapeutics, Urticaria, Survey

Introduction

Urticaria is a group of diseases characterized by the development of wheals, angioedema, or both, that affects between 0.3% and 20% of the population worldwide (Parisi et al., 2018).

Its definition, classification, and management have been controversial. However, there are international guidelines that have been published and recently revised and updated (Zuberbier et al., 2018). According to them, acute spontaneous urticaria is defined as the occurrence of the disease for less than 6 weeks. When it lasts longer, it is considered a chronic condition (Antia et al., 2018). This distinction is crucial because acute urticaria does not usually require a diagnostic work up. On the other hand, patients with chronic urticaria (CU) have to be evaluated in order to identify triggers, rule out differential diagnoses, and assess disease activity, since the available data indicates that this disease can affect quality of life (Zuberbier et al., 2018). Either in acute or chronic cases, the goal of treatment is to manage the symptoms until the disease is gone. The therapeutic approach involves the identification and elimination of underlying causes, the avoidance of eliciting factors, and pharmacological treatment that pursues to reduce the effect of mast cell mediators such as histamine (Antia et al., 2018).

Although there are multiple available pharmacological therapies, H1 antihistamines are still the most widely prescribed drugs for the treatment of CU. Current guidelines recommend non-sedative H1 antihistamines as first and second-line treatments, and omalizumab for refractory cases (Zuberbier et al., 2018). However, it has been described that these

recommendations are not universally taken into account (Firooz et al., 2019; Gómez et al., 2019; Ho et al., 2019).

Understanding the trends in CU management among dermatologists in a real world setting might allow for the development of strategies to optimize it in the future. The aim of this study was to estimate the percentage of dermatologists who take an optimal approach to CU, according to international guidelines, and to explore the variables associated with optimal management.

Participants and Method

Study design and Setting

This cross-sectional study was conducted using an anonymous, voluntary, 17-question survey specifically designed by the authors (Figure 1). The survey was delivered by email to board certified dermatologists from 24 provinces in Argentina, between June 1, 2018, and October 30, 2018.

The definitions of optimal treatment were in accordance with the EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria (Zuberbier et al., 2018). Optimal first-line treatment for patients with CU was defined as the prescription of non-sedative H1 antihistamines. Optimal second-line treatment for patients with CU was stated as an increase in the dosage of antihistamines of up to four times the initial dose. Optimal third-line treatment for patients with CU was considered to be the prescription of omalizumab in refractory cases. Therefore, for the purpose of this study, we defined a suboptimal approach to CU as any situation where dermatologists chose a drug other than those suggested in the international guidelines (Zuberbier et al., 2018).

The survey collected the following information: dermatologists' demographic information including age, the state and region where they practice dermatology (urban vs. non-urban), number of years of experience in dermatology, their knowledge regarding urticarias'

definition and etiology, their usual routine work up for this pathology, and the drugs that they use to treat urticaria in a first, second or third-line treatment.

The following dermatologists variables were collected as potential explanatory variables associated with suboptimal treatment management: age, years of expertise in their specialty, and overall knowledge of the disease. The latter was defined by the simultaneous presence of 3 concepts: knowledge of CU definition (known as a condition characterized by the development of wheals, angioedema, or both that lasts for less than 24 hours for at least 6 weeks), knowledge of the existence of the 7-day urticaria activity score (UAS7), and knowledge that CU impacts quality of life.

In Argentina during the period of the study, the drugs that were available for the treatment of CU were loratadine, desloratadine, cetirizine, levocetirizine and fexofenadine, hydroxyzine, diphenhydramine, meprednisone, betametasona, ranitidine, montelukast, cyclosporine, methotrexate, and omalizumab. Rupatadine, ebastine or bilastine were not available.

The STROBE statement was followed to report our research.

Statistical Analysis

Categorical data is presented in absolute numbers and percentages. Continuous data is presented as median with interquartile range 25%-75% (IQR). In order to explore factors associated with an optimal approach to the first, second and third-line treatment of patients with CU, we performed a logistic regression analysis. Candidate variables included in the model were the dermatologists' age, years of expertise in their specialty and overall knowledge of the disease as previously defined. The association of each of these variables with the outcome is presented with their crude and adjusted odds ratios (OR), and their corresponding 95% confidence intervals (CI). All tests were two-sided. Statistical significance was declared for a p value <0.05. STATA software (StataCorp. version 14.2) was used for statistical calculations.

Results

Study Group Characteristics and Knowledge of the Disease

The survey was delivered to 450 dermatologists of whom 165 agreed to participate in the study and answered it. Most of them were less than 40 years old, had at least 5 years of experience in dermatology, and worked in an urban setting. All of them treated patients with urticaria by the time they were completing the survey (Table 1).

With respect to their knowledge of the disease's definition, 132 (80%) dermatologists correctly stated the definition of CU, 56 (34%) knew what the UAS7 was, and all answered that they were aware that urticaria affects quality of life (Table 1). A total of 55 (33%) dermatologists fulfilled the criteria of overall knowledge of the disease.

Diagnostic Work Up in Patients with Chronic Urticaria

With respect to the medical interview approach, half of the participants intended to identify the disease through the relationship between the clinical manifestations and the different triggers as stated in the guidelines. Moreover, almost all participants reported that they perform a complete blood count and an erythrocyte sedimentation rate in the initial laboratory work up as suggested by the guidelines. However, most of the physicians also ordered additional tests as described in Table 2. Nevertheless, the vast majority of the dermatologists could not identify a clear etiology of CU in their patients (Table 1).

Choice of Treatment

The percentage of dermatologists who performed an optimal first, second and third-line treatment approach was 50.0 % (95%CI 42.0%-57.3%), 35.1 (95%CI 28.2%-42.3%), and 14.5% (95%IC 9.9%-20.8%), respectively (Table 2).

With respect to the group of dermatologists that chose a suboptimal first-line treatment for this disease, a total of 82 (50%) dermatologists prescribed a suboptimal first-line treatment: 66 (40%) chose sedative H1 antihistamines, 34 (21%) oral corticosteroids, 6 (3.6%) montelukast, 4 (2.4%) cyclosporine and 1 (0.6%) omalizumab.

Of the 107 (65%) dermatologists who chose a suboptimal second-line treatment for CU, 74 (45%) selected to increase the dosage of the non-sedative H1 antihistamines, but they also decided to add another drug such as montelukast or corticosteroids. Additionally, 73 participants (44%) stated that they prefer to combine two different antihistamines, 37 (22.5%) chose to add corticosteroids, and 22 (13%) to add H2 antihistamines.

Of the 141 (85%) dermatologists who chose a suboptimal third-line treatment, 21 (13%) prescribed cyclosporine and 10 (6%) methotrexate. Twenty-three (14%) dermatologists stated that they consider the same to choose omalizumab, cyclosporine or methotrexate. Interestingly, of the 23 dermatologists who considered omalizumab along with other third-line therapies, 19 were dermatologists between 25 and 40 years old, 2 were between 41 and 55 years old, and 2 were over 55 years old.

While considering the three lines of treatment, out of all of the 165 dermatologists, only 9 (5%) chose an optimal overall treatment that follows the international guidelines recommendations for the management of CU.

Variables Associated with the Optimal Treatment Approach

The crude association between the participants' age, years of experience as a professional, and overall knowledge of the disease with the selection of an optimal first, second and third-line treatment is shown in Table 3. The data shows the lack of association between these explanatory variables with the optimal first and third-line treatments. However, with respect to the prescription of the second-line treatment the three variables were associated with an optimal approach (Table 3). In the multivariate analysis variables that remain associated were: age older than 55 years old (OR: 0.12, CI: 0.01-0.99, p 0.005) and those with more than five years of expertise in dermatology (OR: 0.4, CI: 0.19-0.81, p 0.001). This means that older dermatologists and those with more years of experience were less likely to perform an optimal approach in second-line treatment.

Discussion

This study's main finding is that most of the Argentine dermatologists who answered the survey manage patients with CU in disagreement with international guidelines (Zuberbier et al., 2018). To the best of our knowledge, this is the second study that has examined the dermatologists approach to and management of patients with CU in Latin America. Cherrez et al. in Ecuador performed the first one. (Cherrez et al., 2017)

Regarding the knowledge of the disease's definition, surprisingly 1 out of 5 dermatologists could not accurately define CU. This result shows a lack of knowledge that should be taking into account to plan educational activities.

International guidelines recommend searching for possible triggers by asking appropriate questions and performing basic tests (differential blood cell count, reactive protein C, and/or erythrocyte sedimentation rate), only considering additional diagnostic measures based on the patient's history and the physical examination (Zuberbier et al., 2018). Interestingly, most of the dermatologists ordered these basic tests, but also requested additional ones that were not suggested by the guidelines, including the HIV test, antinuclear antibodies, and patch tests, among others. In spite of this, less than 20% of the dermatologists reported that they were able to identify an underlying CU trigger in more than 1 out of 4 of their cases. Cherrez Ojeda et al. and Weller et al reported similar findings. (Cherrez Ojeda et al., 2010; Weller et al., 2013). This supports expert's recommendations, which strongly discourage the use of intensive and costly screening tests to identify CU triggers or aggravating factors (Weller et al., 2013; Zuberbier et al., 2018).

A baseline assessment of CU activity and its impact on patient quality of life with patients reported outcomes instruments is essential for guiding treatment decisions. (Zuberbier et al., 2018). However, only 1 out of 3 physicians knew what the UAS7 was. Interestingly, these findings were similar to those that have been reported by Cherrez-Ojeda et al. and Bernstein et al. Therefore, this data indicates a knowledge gap that should be bridged with future educational efforts. (Bernstein JA et al., 2018; Cherrez-Ojeda I et al., 2019).

Antihistamines are considered first-line treatment for patients with CU. First generation or sedative antihistamines result in pronounced adverse reactions and many interactions with

other drugs and alcohol. On the other hand, modern second generation or non-sedative antihistamines are safe drugs with minimal adverse effects. Thus, international guidelines strongly recommend against using the former to manage CU and suggest that the latter should be considered as the first line treatment for the symptoms of this pathology due to their good safety profile. In our survey, non-sedative antihistamines were preferred for starting the therapy by half of the physicians. Interestingly, this preference was not related to the dermatologists' age, years of experience, or overall knowledge of the disease. Moreover, around one third of the respondents began therapy with sedative antihistamines and one fifth selected systemic steroids instead. Although no statistically significant association was found, the selection of sedative antihistamines seems to be related to the physician's age, since 36% of the dermatologists between the ages of 25 and 40 years old prescribe them, while the percentage rises to 43% among the participants between the ages of 41 and 55 years old, and up to 62% among those older than 55 years old. Since sedative H1 antihistamines and steroids are actually considered by experts to be obsolete for the long-term management of CU, it is remarkable that they were chosen by a significant number of dermatologists. Weller et al., from Germany, report that sedative H1 antihistamines and oral steroids were also used as a first choice treatment by a considerable percentage of physicians (19.2% and 14.6%), which is a smaller amount than in our survey (Weller et al., 2013). Some authors state that this could be explained by the fact that many professionals considered that sedative antihistamines and corticosteroids are safer because of their long-standing use (Weller et al., 2013; Zuberbier et al., 2018).

International guidelines recommend increasing the dosage of non-sedative H1 antihistamines as second line treatment, as supported by clinical experience and research studies (Choonhakarn et al., 2018; Weller et al., 2013; Zuberbier et al., 2018). In the survey, about one third of the physicians stated that they would proceed as the recommendations suggest. Interestingly, these participants were younger and had less years of training than participants who performed a suboptimal approach. Perhaps, this fact may be related to the recent advances in the knowledge of the disease and the most updated training that medical students receive on this topic during college and their dermatology residency.

Accepted Article

Compared to Weller et al. results, the choices of Argentine dermatologists when selecting first and second-line treatments seem to be similar to those of German dermatologists. Furthermore, we have compared our results to a comparable research performed in Ecuador and found that the Argentine physicians were more likely to prescribe optimal first (50% vs. 30%) and second-line medical care (35% vs. 12.9%)(Weller et al., 2013; Cherrez et al., 2017).

Currently, international guidelines suggest the addition of omalizumab for those patients with CU who are refractory to high doses of non-sedative H1 antihistamines (Zuberbier et al., 2018). Remarkably, only 15% of the physicians chose this drug as a third line therapy. We could not find an association between this decision and other variables, but, noticeably, none of the participants older than 55 years old prescribed this drug. Although omalizumab was approved in our country for CU in 2014, our study shows that in a real-life practice setting, experience with omalizumab is still scarce. Weller et al. and Maurer et al. have reported similar findings (Maurer et al., 2018, Weller et al., 2013).

This study analyzes factors that could be major associated with the approach to patients with CU. It provides helpful information and reinforces previous findings. Moreover, it highlights the importance of the continual medical education on CU to keep physicians updated.

One of our study's limitations is that it was performed through a voluntary survey delivered by email, so a selection bias is likely to have occurred. It can be assumed that physicians more used to using internet are more likely to take part in this kind of research. This might affect the generalizability of our results to the general population of dermatologists, but we believe that this limitation does not essentially change our results. Another potential limitation is that there is not an accepted definition of knowledge of a given disease. Therefore, we came with a definition that was specifically major built for the purpose of this study. This definition was considered by all the investigators to be an acceptable proxy of the basics aspects of CU that a physician needs to know about the proper management of this disease.

In conclusion, the real-life approach and treatment of patients with CU in medical practice

Accepted Article

settings in Argentina is only partially in agreement with international guidelines. Accordingly, it can be assumed that the dermatologists are not well informed about these updated guidelines. Understanding these educational needs will allow us to develop teaching programs that might enable the international guidelines for managing CU patients to be implemented and the best clinical practices to be reached.

References

Antia C, Baquerizo K, Korman A, Bernstein JA, Alikhan A (2018). Urticaria: A comprehensive review: Epidemiology, diagnosis, and work up. *J Am Acad Dermatol*, 79, 599–614.

Bernstein JA, Kavati A, Tharp MD, Ortiz B, MacDonald K, Denhaerynck K, Abraham I. (2018). Effectiveness of omalizumab in adolescent and adult patients with chronic idiopathic/spontaneous urticaria: a systematic review of 'real-world' evidence. *Expert Opin Biol Ther*, 18, 425–448.

Cherrez A, Maurer M, Weller, Calderon JC, Simancas-Racines D, Cherrez-Ojeda I (2017). Knowledge and management of chronic spontaneous urticaria in Latin America: a cross-sectional study in Ecuador. *World Allergy Organ J*, 10, 21.

Cherrez Ojeda I, Vanegas E, Felix M, Mata V, Cherrez S, Simancas-Racines D... Calderon JC (2018). Etiology of chronic urticaria: the Ecuadorian experience. *World Allergy Organization Journal* 11,1.

Cherrez-Ojeda I, Maurer M, Bernstein JA (2019). Learnings from real-life experience of using omalizumab for chronic urticaria in Latin America. *World Allergy Organization Journal*, 12, 100011.

Choonhakarn C, Chaowattanapanit S, Julianon N (2018). The treatment outcomes and dose de-escalation of desloratadine up-dosing in chronic spontaneous urticaria. *Int J Dermatol*, 57, 423–7.

Firooz A, Akhlaghi A, Golbidi P, Pourjafari M, Abdollahimajd F, Azimi H...Teymori G (2019). Real life management of chronic urticaria: Multicenter and cross sectional study on patients and dermatologists in Iran. *Dermatol Ther*, 32, e12796.

Gómez RM, Jares E, Borges MS, Baiardini I, Canonica GW, Passalacqua G, Lavrut J (2019). Latin American chronic urticaria registry (CUR) contribution to the understanding and knowledge of the disease in the region. *World Allergy Organ J*, 12,100042.

Ho B, Heelan K, Solman L, Jones R, Dua J, Ingram JR, Flohr C (2019). A survey of the

treatment and management of patients with severe chronic spontaneous urticaria. *Clin Exp Dermatol*, 44, 353-355.

Larenas-Linnemann DES, Parisi CAS, Ritchie C, Cardona-Villa R, Cherrez-Ojeda I, Cherrez A...Caraballo JMS (2018). Update on Omalizumab for Urticaria: What's New in the Literature from Mechanisms to Clinic. *Curr Allergy Asthma Rep*, 18, 33.

Maurer M, Houghton K, Costa C, Dabove F, Ensina LF, Giménez-Arnau A...Chapman-Rothe N (2018). Differences in chronic spontaneous urticaria between Europe and Central/South America: results of the multicenter real world AWARE study. *World Allergy Organ J*, 16, 32.

Parisi CA, Ritchie C, Petriz, Torres CM, Gimenez-Arnau A (2018) Chronic urticaria in a health maintenance organization of Buenos Aires, Argentina - new data that increase global knowledge of this disease. *An Bras Dermatol*, 93,76–9.

Weller K1, Viehmann K, Bräutigam M, Krause K, Siebenhaar F, Zuberbier T, Maurer M (2013). Management of chronic spontaneous urticaria in real life - in accordance with the guidelines? A cross-sectional physician-based survey study. *J Eur Acad Dermatol*, 27, 43–50.

Zuberbier T, Aberer W, Asero R, Abdul Latiff AH, Baker D, Ballmer-Weber B...Maurer M (2018). The EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. *Allergy*, 73, 1393–414.

Table 1. Dermatologists' demographic information and knowledge of chronic urticaria (n=165)

Variable	Result, n (%)
Age	
<40 years	110 (67)
41-55 years	42 (25)
>55 years	13 (8)
Years of specialty	
<5 years	66 (40)
5-15 years	70 (42)
>15 years	29 (18)
Geographical area of practice ¹	
Urban	136 (94)
Not urban	8 (6)

Age range of attended patients ²

Adult patients	95 (58)
Pediatric patients	1 (1)
Adult and pediatric patients	68 (41)

Treat patients with urticaria 165 (100)

Treat patients with angioedema 104 (63)

Overall knowledge of the disease 55 (33)

Knowledge of CU definition ²	132 (80)
Knowledge that CU impacts quality of life ²	164 (100)
Knowledge of UAS7 ²	56 (34)

CU as a self-limiting disease ² 18 (11)

Identify an underlying cause of CU

Less than 30% of cases	138 (83)
31-50% of cases	19 (12)
51-70% of cases	5 (3)
More than 71% of cases	3 (2)

¹ Available in 144 dermatologists

² Available in 164 dermatologists

Abbreviations: CU, chronic urticaria; UAS7, urticaria activity score.

Table 2. Diagnostic work up and choice of treatment of dermatologists in chronic urticaria (n=165).

Variable	Results n (%)
Medical interview approach (including drugs or food consumption, insect bites, allergen exposure, systemic diseases, physical triggers)	87 (53)
Laboratory tests	
Complete blood count	161 (98)

Erythrocyte sedimentation rate	153 (93)
Renal function (urea and creatinine)	133 (81)
Glycaemia	129 (78)
Liver tests	144 (87)
Complete urine test	99 (60)
Parasitological examination of stool	120 (73)
Image studies	27 (16)
Serum total tryptase	31 (19)
Immunoglobulin E levels	127 (77)
Antinuclear antibody test	135 (82)
Serum TSH concentration	134 (81)
Antithyroid antibodies	108 (65)
HIV antibodies	121 (73)
Hepatitis B and hepatitis C antibodies	122 (74)
Specific provocation tests for physical triggers	51 (31)
Patch test	41 (25)
Prick test	26 (16)
Optimal treatment according to international guidelines	
Optimal first line treatment	82 (50)
Optimal second line treatment	58 (35)
Optimal third line treatment	24 (15)
Global optimal treatment (first, second and third line)	9 (5)

¹ Available in 164 dermatologists

Table 3. Comparison of dermatologists characteristics according to their choice of first, second and third line treatment for chronic urticaria (n=165).

Variable	Not optimal treatment n (%)	Optimal treatment n (%)	OR	95% CI	p
First line treatment	N=83	N=82			
Age					
Age 25-40 years	52 (62,6)	58 (70.7)	ref	ref	ref
Age 41-55 years	23 (27.7)	19 (23.2)	0.74	0.36-1.51	0.41
Age >55 years	8 (9.6)	5 (6.1)	0.56	0.17-1.82	0.33
Years of expertise					
<5 years	28 (34)	38 (46)	ref	ref	ref
5-15 years	36 (44)	34 (41)	0.74	0.37-1.45	0.38
>15 years	18 (22)	11 (13)	0.67	0.28-1.63	0.38
Overall knowledge of the disease					
Participants with overall knowledge	23 (27.7)	32 (39)	1.67	0.87-3.21	0.12
Second line treatment	N=107	N=58			
Age					
Age 25-40 years	66 (61.9)	44 (75.9)	ref	ref	ref
Age 41-55 years	29 (27.1)	13 (22.4)	0.67	0.31-1.43	0.30

Age >55 years	12 (11.2)	1 (1.8)	0.12	0.01-0.99	0.005
Years of expertise					
<5 years	33 (30.9)	33 (56.9)	ref	ref	ref
5-15 years	50 (46.7)	20 (34.5)	0.40	0.19-0.81	0.001
>15 years	24 (22.4)	5 (8.6)	0.21	0.071-0.61	0.004
Overall knowledge of the disease					
Participants with overall knowledge of the disease	29 (27.1)	26 (44.8)	2.18	1.12-4.27	0.02
Third line treatment	N=141	N=24			
Age					
Age 25-40 years	95 (67.4)	15 (62.5)	ref	ref	ref
Age 41-55 years	33 (23.4)	9 (37.5)	1.73	0.69- 4.31	0.24
Age >55 years	13 (9.2)	0 (0)	_*	_*	_*
Years of expertise					
<5 years	59 (41.8)	7 (29.2)	ref	ref	ref
5-15 years	54 (38.3)	16 (66.7)	2.49	0.95-6.53	0.06
>15 years	28 (19.9)	1 (4.2)	0.3	0.35-2.56	0.27
Overall knowledge of					

the disease

Participants with overall knowledge of the disease	44 (31.2)	11 (45.8)	1.86	0.77-4.49	0.16
--	-----------	-----------	------	-----------	------

** Since there is no variability in one of the strata, this OR cannot be determined

Figure 1. Chronic Urticaria National Survey

- 1- Select your age:**
- 25-40 years
 - 41-55 years
 - >55 years
- 2- Select the number of years that you have been working as a specialist in dermatology.**
- <5 years
 - 5-15 years
 - >15 years
- 3- Where do you practice dermatology?**
- Urban geographical area with more than 20,000 inhabitants.
 - Not urban geographical area with more than 20,000 inhabitants.
- 4- Most of the patients you attend are?**
- Pediatrics patients
 - Adults patients
 - Both pediatrics and adults patients
- 5- Do you treat patients with urticaria?**
- Yes
 - No
- 6- Do you treat patients with angioedema?**
- Yes
 - No
- 7- Do you think that chronic urticaria is defined as a process that lasts...**
- more than 2 weeks
 - more than 4 weeks
 - more than 6 weeks
 - more than 12 weeks
 - more than 6 months
- 8- During the medical interview of patients with chronic urticaria, what do you ask them about: (Select all what you consider appropriate)**
- Drug consumption prior to the onset of chronic urticaria
 - Food consumption prior to the onset of chronic urticaria
 - Insect bites prior to the onset of chronic urticaria
 - Allergen exposure prior to the onset of chronic urticaria
 - Signs and symptoms of systemic diseases
 - Physical triggers such as heat, cold, exercise, pressure, water, sun, etc.
- 9- In those cases that you consider that the patients have chronic urticaria, what complementary studies do you request?: (Select all what you consider appropriate)**
- Complete blood count
 - Erythro sedimentation rate
 - Renal function (urea and creatinine)
 - Glycemia
 - Liver tests
 - Complete urine test
 - Parasitological examination of stool
 - Serum total tryptase
 - Immunoglobulin E levels
 - Antinuclear antibody test
 - Serum TSH
 - Antithyroid antibodies
 - HIV serologic test
 - Hepatitis B and hepatitis C serologic tests
 - Specific provocation tests for physical triggers
 - Patch test
 - Prick test
- 10- Do you consider that you can identify an underlying cause of chronic urticaria in:**
- Less than 10% of cases?
 - 11-30% of cases?
 - in 31-50% of cases?
 - 51-70% of cases?
 - more than 71% of cases?
- 11- To start the treatment of a patient with chronic urticaria, you usually choose: (If you usually choose combined treatments, select all the options that are you consider appropriate)**
- Oral diphenhydramine
 - Endovenous diphenhydramine
 - Hydroxyzine
 - Loratadine
 - Desloratadine
 - Cetirizine
 - Levocetirizine
 - Fexofenadine
 - Oral meprednisone
 - Oral Betamethasone
 - Intramuscular dexamethasone
 - Cyclosporine
 - Montelukast
 - Omalizumab
 - Other:
- 12- If the patient does not improve with the treatment for urticaria that you have indicated in the first place, your next step is: (If you usually choose combined treatments, select all the options that are you consider appropriate)**
- Increase the dose of the antihistamine you chose
 - Combine two different antihistamines
 - Increase the dose of corticosteroids
 - Change treatment to another antihistamine
 - Add corticosteroids to the antihistamine
 - Add anti H2 antihistamines, like ranitidine
 - Add antileukotrienes, like montelukast
 - Add cyclosporine
 - Add omalizumab
 - Add methotrexate
 - Other:
- 13- If your decision was to increase the antihistamine dose, you increase the dose:**
- Twice the initial dose
 - Three times the initial dose
 - Four times the initial dose
- 14- If the patient does not improve with this second line of treatment for urticaria that you have prescribed, which is your next step?**
- Increase the dose of the antihistamine you chose
 - Combine two different antihistamines
 - Increase the dose of corticosteroids
 - Change treatment to another antihistamine
 - Add anti H2 antihistamines, like ranitidine
 - Add antileukotrienes, like montelukast
 - Add corticosteroids to the antihistamine
 - Add cyclosporine
 - Add omalizumab
 - Add methotrexate
 - Other:
- 15- Do you consider that chronic urticaria affects patient's quality of life?**
- Yes
 - No
- 16- Do you consider that chronic urticaria is a self-limiting disease?**
- Yes
 - No
 - Sometimes
 - Maybe
- 17- Do you know what UAS7 score is?**
- Yes
 - No