Allergol Immunopathol (Madr). 2016;xxx(xx):xxx-xxx

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

www.elsevier.es/ai

ORIGINAL ARTICLE

# Management of chronic spontaneous urticaria in routine clinical practice: A Delphi-method questionnaire among specialists to test agreement with current European guidelines statements

A. Giménez-Arnau[a], M. Ferrer[b,*], J. Bartra[c], I. Jáuregui[d], M. Labrador-Horrillo[e], J. Ortiz de Frutos[f], J.F. Silvestre[g], J. Sastre[h], M. Velasco[i], A. Valero[j]

[a] *Dermatology Service, Hospital del Mar, Parc de Salut Mar, Universitat Autonoma Barcelona [Autonomous University of Barcelona], Barcelona, Spain*
[b] *Allergology Department, Clínica Universidad de Navarra [University Clinic of Navarra], Pamplona, Spain*
[c] *Pneumology and Allergy Service, Hospital Clinic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) [August Pi i Sunyer Biomedical Research Institute], Barcelona, Spain*
[d] *Allergology Service, Hospital Universitario Basurto [Basurto University Hospital], Bilbao, Spain*
[e] *Allergology Section, Medicine Department, Hospital Vall d'Hebron, Universitat Autònoma de Barcelona [Autonomous University of Barcelona], Barcelona, Spain*
[f] *Dermatology Service, Hospital Universitario 12 de Octubre [University Hospital 12 of October], Madrid, Spain*
[g] *Dermatology Service, Hospital General Universitario de Alicante [University of Alicante General Hospital], Alicante, Spain*
[h] *Allergology Service, Fundación Jiménez Diaz [Jiménez Diaz Foundation], Madrid, Spain*
[i] *Dermatology Service, Hospital Arnau de Vilanova, Valencia, Spain*
[j] *Pneumology and Allergy Service, Hospital Clinic (ICT), University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) [August Pi i Sunyer Biomedical Research Institute], Barcelona, Spain*

Received 2 March 2016; accepted 13 June 2016

**KEYWORDS**
Urticaria;
Angio-oedema;
Consensus;
Delphi;
Delphi technique;
Omalizumab

**Abstract**
*Background:* Chronic spontaneous urticaria (CSU) is a frequent clinical entity that often presents a diagnostic and therapeutic challenge.
*Objective:* To explore the degree of agreement that exists among the experts caring for patients with CSU diagnosis, evaluation, and management.
*Methods:* An online survey was conducted to explore the opinions of experts in CSU, address controversial issues, and provide recommendations regarding its definition, natural history, diagnosis, and treatment. A modified Delphi method was used for the consensus.
*Results:* The questionnaire was answered by 68 experts (dermatologists, allergologists, and primary care physicians). A consensus was reached on 54 of the 65 items posed (96.4%). The experts concluded that CSU is a difficult-to-control disease of unpredictable evolution. Diagnostic tests

* Corresponding author.
*E-mail address:* mferrerp@unav.edu (M. Ferrer).

http://dx.doi.org/10.1016/j.aller.2016.06.007


Please cite this article in press as: Giménez-Arnau A, et al. Management of chronic spontaneous urticaria in routine clinical practice: A Delphi-method questionnaire among specialists to test agreement with current European guidelines statements. Allergol Immunopathol (Madr). 2016. http://dx.doi.org/10.1016/j.aller.2016.06.007

should be limited and based on clinical history and should not be indiscriminate. Autoinflammatory syndromes and urticarial vasculitis must be ruled out in the differential diagnosis. A cutaneous biopsy is only recommended when wheals last more than 24 h, to rule out urticarial vasculitis. The use of specific scales to assess the severity of the disease and the quality of life is recommended. In patients with severe and resistant CSU, second-generation H1-antihistamines could be used at doses up to four times the standard dose before giving second-line treatments. Omalizumab is a safe and effective treatment for CSU that is refractory to H1-antihistamines treatment. In general, diagnosis and treatment recommendations given for adults could be extrapolated to children.

*Conclusions:* This work offers consensus recommendations that may be useful in the management of CSU.



## Introduction

Urticaria is a cutaneous disease characterised by the appearance of wheals, angio-oedema, or both.[1] It is estimated that 8–20% of the population is likely to experience at least one episode of acute urticaria,[1,2] and 0.6–1.8% of the population is likely to experience an episode of chronic urticaria during their life. Chronic urticaria, defined as daily or almost daily outbreaks for more than six weeks, may significantly affect the quality of patients' life and their daily activities and performance.[1] Pruritus, interference with sleep, lesions on visible body parts, or difficulty moving the joints of the ankles or the hands can become disabling.

In recent years, advances in the understanding of the pathogenesis of urticaria, updates of management guidelines, improved diagnostic techniques, and the advent of highly relevant therapeutic advances have highlighted the morbidity of chronic urticaria. According to the latest classification of the European Academy of Allergy and Clinical Immunology (EAACI), chronic urticaria comprises inducible urticarias (among which are the physical urticarias) and chronic spontaneous urticaria (CSU) (Table 1). The treatment of CSU can be frustrating for both patients and physicians because the lesions may persist, despite the use of existing treatments.[2] Recently, the use of omalizumab, a humanised monoclonal anti-IgE antibody, has been approved for the treatment of CSU. It is capable of controlling the symptoms of CSU in a significant number of patients who are non-responders to high dose antihistamines in a monotherapy regimen or in combination with other drugs.[1] Its safety and efficacy have been demonstrated in randomised placebo-controlled clinical trials where it was used when antihistamines (H1 and H2) or leukotriene receptor antagonists (LTRA) were proven to be ineffective.[4–6]

**Table 1** Classification of chronic urticaria.

| Subtypes of chronic urticaria | |
|---|---|
| Chronic spontaneous urticaria | Inducible urticaria |
| Spontaneous appearance of wheals, angio-oedema, or both lasting ≥6 weeks | Physical urticaria<br>– Symptomatic dermographism<br>– Cold urticaria<br>– Delayed pressure urticaria<br>– Solar urticaria<br>– Heat urticaria<br>– Vibratory angio-oedema<br>Cholinergic urticaria<br>Contact urticaria<br>Aquagenic urticaria |

This document addresses the management of CSU by focusing on its natural history and diagnosis, its clinical evaluation and follow-up, and its treatment in routine clinical practice. After consensus was reached, some recommendations that can facilitate the clinical management of this disease were developed. Our aim was to study the degree of consensus that the recently published European guidelines have among the specialists in Dermatology and Allergy. The analysis of the results of this work will contribute to the current knowledge of a frequent disease in emergency rooms, primary care, internal medicine, and allergology and dermatology. This analysis will contribute to the proper management of the patient from the start of clinical occurrence, achieving thus better control of the disease and reducing its social and economic impact.

## Materials and methods

### The Delphi method

A modified Delphi method was used in this study.[7] According to this method, the opinions of a panel of experts were anonymously requested through the use of an online questionnaire in two rounds of voting. The questionnaire consisted of assertions or items that addressed some controversial aspects about CSU and were scored according to the degree of the panelists' agreement or disagreement with them. The results obtained were statistically analysed, and the results of the first vote were circulated among the participants. The items on which there was no consensus were re-circulated and subjected to a second round of voting. In this manner, the experts could reconsider their responses in the light of the pooled results. The results obtained in this second round were statistically analysed to determine which issues had finally achieved a sufficient degree of consensus among the experts, and whether or not they were in agreement or in disagreement with each item presented.

Please cite this article in press as: Giménez-Arnau A, et al. Management of chronic spontaneous urticaria in routine clinical practice: A Delphi-method questionnaire among specialists to test agreement with current European guidelines statements. Allergol Immunopathol (Madr). 2016. http://dx.doi.org/10.1016/j.aller.2016.06.007