Clinical Management Review

A Comparison of the United States and International Perspective on Chronic Urticaria Guidelines

Torsten Zuberbier, MD[a], and Jonathan A. Bernstein, MD[b] *Berlin, Germany; and Cincinnati, Ohio*

Urticaria is a heterogeneous skin disorder that may be acute or chronic and is defined by the appearance of wheals, angioedema, or both. The European perspective is expressed in a recent international guideline and the American perspective has been based on the US Joint Task Force chronic urticaria practice parameter published in 2014. Both the international guideline (initiated by the European societies European Academy of Allergology and Clinical Immunology [EAACI]/Global Allergy and Asthma European Network [GA^{2}LEN]/European Dermatology Forum [EDF] in collaboration with the World Allergy Organization [WAO]) and the US (American Academy of Allergy, Asthma & Immunology/American College of Allergy, Asthma and Immunology) guideline have been developed to help direct primary care physicians and specialists in the management of their patients with urticaria. The EAACI/GA^{2}LEN/EDF/WAO guideline applied the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach to developing consensus recommendations and these were then discussed in a Delphi conference including more than 250 specialists in the field and have been endorsed by more than 40 international societies. In contrast, the US Joint Task Force CU practice parameter made recommendations based on scientific evidence whenever possible; however, when there was insufficient evidence, recommendations were based on expert consensus opinion. Although both agree on most points regarding the definition, general evaluation, and treatment, there are some differences that exist between the 2 guidelines. Most of these differences pertain to recommendations based on expert opinion because of weak scientific evidence. Within this document, we compare the recommendations of these 2 groups, highlighting the key similarities and differences. © 2018 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2018;■:■-■)

Key words: *Urticaria; Angioedema; Guidelines; International; United States; Joint Task Force; Scientific evidence; Evaluation; Treatment*

INTRODUCTION

In 2000 the first European guideline based on a consensus conference was developed.[1,2] In December 2016, the fifth conference was organized to create an international, global guideline. Initiated by the European Academy of Allergology and Clinical Immunology in conjunction with the European Dermatology Forum, the Global Allergy and Asthma European Network, and the World Allergy Organization, all international societies were invited to participate.[3,4] A driving force behind the idea of the development of this guideline was to achieve a worldwide consensus on the principles of classification, diagnosis, and treatment of urticaria, which could subsequently be adapted by urticaria experts in different regions of the world through the involved parent organization. Altogether, 42 allergy/dermatology national and international societies representing 94 countries participated in the updated guideline. The North American and South American societies included were the American Academy of Allergy, Asthma & Immunology (AAAAI), the American Academy of Dermatology, the American College of Allergy, Asthma and Immunology (ACAAI), the Brazilian Association of Allergy and Immunopathology, the Mexican College of Clinical Immunology and Allergy, the Canadian Society of Allergy and Clinical Immunology, the Brazilian Society of Dermatology, and the Latin American Society of Allergy and Immunology.[3,4] In this review, we therefore refer to it as an international guideline.

Unique to all current urticaria guidelines, the international urticaria guideline has used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, which is considered the most rigorous and comprehensive methodology for scientific evidence-based guidelines.[3] The guideline was prepared by a panel consisting of delegates of each

[a]Department of Dermatology and Allergy, Charité - Universitätsmedizin Berlin, Berlin, Germany
[b]University of Cincinnati College of Medicine, Cincinnati, Ohio

Conflicts of interest: T. A. Zuberbier has received consultancy fees, research support, and/or honoraria from AstraZeneca, AbbVie, ALK, Almirall, Astellas, Bayer Health Care, Bencard, Berlin Chemie, FAES, HAL, Henkel, Kryolan, Leti, L'Oreal, Meda, Menarini, Merck, Merck Sharp Dohme, Novartis, Pfizer, Sanofi, Stallergenes, Takeda, Teva, and UCB; is a committee member of the World Health Organization initiative "Allergic Rhinitis and its Impact on Asthma" (ARIA); is a Member of the Board, German Society for Allergy and Clinical Immunology (DGAKI); is Head, European Centre for Allergy Research Foundation (ECARF); is Secretary General, Global Allergy and Asthma European Network (GA^{2}LEN); and is a Member, Committee on Allergy Diagnosis and Molecular Allergology, World Allergy Organization. J. A. Bernstein has received research support, consultancy fees, and travel support from AstraZeneca, Novartis, Genentech, and Allkalos; is on the boards for Hereditary Angioedema Association medical advisory board, American Academy of Allergy, Asthma & Immunology Foundation Council, UCARE, joint task force, Interasma, and Allergists for Israel; has received consultancy fees from Shire, CSL Behring, Merck, Sanofi-Regeneron, and AstraZeneca; has received lecture fees from Shire, Pharming, Baxalta, and AstraZeneca; has patents with no financial renumeration; has received payment for developing educational presentations from Spire; and is Editor-in-Chief of the *Journal of Asthma*.

Received for publication March 23, 2018; revised April 19, 2018; accepted for publication April 20, 2018.
Available online ■■

Corresponding author: Jonathan A. Bernstein, MD, University of Cincinnati College of Medicine, Division of Immunology/Allergy Section, 231 Albert Sabin Way, ML#563, Cincinnati, OH 45267. E-mail: Jonathan.Bernstein@uc.edu.

2213-2198

https://doi.org/10.1016/j.jaip.2018.04.012

Abbreviations used
CSU- chronic spontaneous urticaria

involved society, which culminated with a large Delphi conference held in Berlin, Germany, including the participation of more than 250 urticaria specialists from all over the world, resulting in the final recommendations that achieved a large global consensus. It was subsequently fully endorsed by the American Academy of Dermatology and the ACAAI and conditionally endorsed by the AAAAI.[3,4]

Although the United States Joint Task Force Urticaria guideline (referred to as the US guideline in this review) published in 2014[5] shares many of the same recommendations as the international guideline, there are several key differences that will be highlighted in this review.[4-6]

METHODOLOGIES USED FOR GENERATING THE INTERNATIONAL AND US GUIDELINES

The updated revised international guideline takes into account the Appraisal of Guidelines Research and Evaluation instrument and the methods suggested by the GRADE working group. The literature review was conducted using the methods given in the Cochrane Handbook for Systematic Reviews of Interventions.[3,7]

Experts from 42 societies were nominated to be involved in the development of the guideline. Initially, key questions and relevant outcomes were selected and rated by the experts using an online survey tool and 23 key questions were identified. A special literature review protocol was developed that specified the literature search strategy. The literature review was conducted on June 1, 2016, and evaluated by 2 independent reviewers who extracted eligible data. After 2 screening phases, 65 studies fulfilling the inclusion criteria were retained. Subsequently, the quality of the evidence following GRADE using GRADEpro Guideline Development Tool (Table I) was assessed.[3,8,9]

Modified evidence-to-decisions (EtD) frameworks were used to assist in judging the size of the desirable and undesirable effects and the balance between these effects, which provided an overview of quality. A recommendation for each evidence-based key question was drafted using standardized wording.

In a preconference online voting round, all GRADE tables, EtD frameworks, and draft recommendations were presented and voted on. The results were either fed back to the expert panel or integrated into the EtD frameworks. All EtD frameworks and draft recommendations were made available to the participants before the consensus conference. In none of the cases was a substantial conflict of interest (high economic or dependency on companies involved in urticaria treatment) observed.[3]

During the conference, all recommendations were voted on by more than 250 participants, all of whom had to submit a declaration that they were an urticaria specialist seeing patients on a regular basis and whether or not they had any conflicts of interest. A nominal group technique was used to achieve consensus on the different recommendations.[3,10]

The consensus conference followed a structured approach, which included presentation of the evidence and draft recommendation, open discussion, initial voting, or collection of alternative wording followed by final voting, if necessary. Voting results were recorded. A strong consensus was defined as more than 90% agreement, whereas 70% to 89% was considered consensus. All recommendations passed with a 75% agreement. An internal and an external review of this process took place. The internal review included the involvement of an international methodologist, supervising the process, and an external review of the manuscript by additional members of all societies involved on the basis of their institutional and national regulations (eg, licensing status of the recommended medication or availability). For example, in the case of the European Dermatology Forum, the review board consisted of 41 members.[3]

TABLE I. Summary of the GRADE approach to assessing the quality of evidence by outcome

High (++++)	We are very confident that the true effect lies close to that of the estimate of effect
Moderate (+++)	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low (++)	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low (+)	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

In contrast, the Joint Task Force practice parameter on chronic urticaria conducted an extensive medical literature search for various terms that were considered relevant to this topic. Literature searches were performed on PubMed, Google Scholar, and the Cochrane Database of Systematic Reviews. All reference types were initially included in the results and references identified as relevant were further searched for relevant references within each article. After acquiring these articles, any relevant references were again searched for and if novel were included in the parameter. In addition, members of the workgroup were asked to provide any references that may have been missed by this initial search. Published clinical studies were rated by category of evidence, which was used to establish the strength of the recommendations. The parameter was subsequently reviewed by designated experts by the AAAAI and the ACAAI. After responding to queries and comments by these reviewers and incorporating changes into the document, the parameter was posted on an open website for all members of the AAAAI and the ACAAI to review and make comments. These comments were responded to by the working group point by point and the parameter was again updated to include any relevant changes or clarifications. Based on this rigorous process, the parameter was believed to represent an evidence-based, broadly accepted consensus document.[5]

DEFINITION AND CLASSIFICATION

Definitions of acute and chronic urticaria do not differ between the guidelines.[4-6] Both agree that less than 6 weeks is acute and more than 6 weeks is chronic urticaria. In general, they define urticaria as the presence of sudden appearance of wheals (with central swelling and surrounding erythema, which are typically pruritic and resolve within about 24 hours) with or without angioedema, defined as a deeper swelling lasting up to 72 hours. Wheals lasting longer than 24 to 48 hours, those that leave hyperpigmentation, or lesions that burn may be vasculitic