CORRESPONDENCE

Severe Asthma Definition, Diagnosis and Treatment

by Prof. Dr. med. Marek Lommatzsch, Prof. Dr. med. Christian J. Virchow
in issue 50/2014

Marginal Effect and Little Clinical Relevance

Although the review by Lommatzsch and Virchow (1) may appear somewhat unsystematic, it at least provides a balanced overview of the basic aspects of the diagnosis and treatment of severe asthma. Therefore, the authors' extremely positive description of the role of omalizumab in severe IgE-mediated asthma that remains inadequately controlled despite treatment with high-dose inhaled corticosteroids (ICS) plus LABA is even more surprising. According to the authors, omalizumab reduces the number of severe exacerbations by 50% while improving the quality of life on top of dramatically reducing the need for corticosteroids and having almost no side effects. An indispensable drug?

A thorough literature search focused on well-designed RCTs tells a different story—a story that is in line with the rather disappointing experiences pulmonologists have made with this drug in clinical practice where treatment with omalizumab showed only a marginal effect and was of little clinical relevance (2). In some studies, the effects were not even statistically significant compared with placebo (3). It is difficult to see why these recent studies from respected research organizations were not included in this review, and why it is not mentioned that in the cited, presumably pivotal study of Humbert et al. (4) the exacerbation rate reduction by just 26% (relative!) became statistically significant only after a statistical adjustment exercise. The authors' advice that treatment with omalizumab is worth a try is difficult to comprehend given the information from the available data and the unpleasant (common and occasional) side effects listed in the prescribing information (Xolair®, July 2014 MS 08/14 V 002), including headache, upper abdominal pain, pharyngitis, syncope, paresthesia, sleepiness, dizziness, orthostatic hypotension, flushes, allergic bronchospasm, cough, dyspepsia, diarrhea, nausea, urticaria, and photosensitivity).

DOI: 10.3238/arztebl.2015.0601a

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adequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. *Allergy* 2005; 60: 309–16.

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Conflict of interest statement

The authors declare that no conflict of interest exists.

Polysomnographic Screening Helpful

This commendable review on severe asthma lists gastroesophageal reflux disease (GERD) as one of the potential comorbidities or triggers for the condition (1). In this context, I would like to highlight the important role of sleep-related breathing disorders, in particular of obstructive sleep apnea (OSA). Odds ratios of 3.6 and, for older asthma patients, even 6.67 have been reported for the association between OSA and the exacerbation of bronchial asthma (2, 3).

Should simple questions asked when taking a patient's history raise the suspicion of OSA, ambulatory polysomnography screening can easily be performed to verify the diagnosis. In case of positive initial findings, further prospective studies will be required to clarify the role of CPAP treatment in improving asthma control (3).

DOI: 10.3238/arztebl.2015.0601b

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Conflict of interest statement

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In Reply:

We like to thank our colleagues Mühlbauer, Sybrecht and Tasci for reading our article (1). In view of the available literature and clinical experience, the role of omalizumab in the treatment of severe asthma has been correctly represented in our article (1). The opinion held by our colleague Mühlbauer that omalizumab is of no pharmacological value is not comprehensible. Likewise, the 'disappointing experiences' our colleague Sybrecht has made with omalizumab cannot be generalized. Frequently, omalizumab treatment achieves

better than expected improvements in clinically relevant parameters, such as exacerbation rate, in carefully phenotyped patients with severe, IgE-mediated asthma. Data from the available studies, which are only superficially cited by our colleagues Mühlbauer and Sybrecht, reflect this situation: In the pivotal study by Humbert et al. published in 2005, a 50% reduction of the incidence of severe exacerbations was observed in patients treated with omalizumab—and that without any “statistical adjustment exercise” (2). For this reason, we mentioned this result in our article (1). In contrast, the study by Bardelas et al. did not have exacerbations, but, among other parameters, an unvalidated, vague 5-point scale, reflecting the impression of the examiner regarding treatment success (IGETE), as an endpoint (3). However, the primary aim of omalizumab treatment is to reduce the incidence of severe exacerbations which is of high clinical relevance especially in patients with severe asthma (4). The commentators’ opinion that treatment with omalizumab is “not even worth a try” in these patients does neither do justice to the scientific evidence, nor is it in line with clinical experience. In addition, it does not reflect the clinical reality of treating patients with omalizumab. To simply provide a list of side effects from the summary of product characteristics is actually misleading: Even the RCTs cited by the authors reported side effects at a placebo level (3). We think that the concerns of Mühlbauer and Sybrecht are proven unfounded by the very studies they have cited. Therefore, we encourage an approach which is not limited to the pharmacological perspective but also draws from clinical experience and insights from real-life studies. Consequently, we continue to recommend to try omalizumab treatment in patients with severe IgE-mediated asthma, as this approach is well supported by both scientific evidence and clinical experience.

We welcome our colleague Tasci’s reference to sleep-related breathing disorder as a comorbidity in patients with asthma and like to point out that this association is highlighted in our article in the “Adherence, triggers, and comorbidities” section (1).

DOI: 10.3238/arztebl.2015.0601c

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Conflict of interest statement

Prof. Lommatzsch has received consultancy and lecture fees and reimbursement of travel and participation costs from Allergopharma, Astra Zeneca, Bencard, Berlin-Chemie, Boehringer-Ingelheim, Chiesi, GSK, Janssen-Cilag, MSD, Mundipharma, Novartis, Nycomed/Takeda, TEVA, and UCB. He has also received fees for commissioned clinical trials from Astra Zeneca and research funding from GSK.

Prof. Virchow has received consultancy and lecture fees and reimbursement of travel and participation costs from Allergopharma, Astra Zeneca, Avontec, Bayer, Bencard, Berlin-Chemie, Bionorica, Boehringer-Ingelheim, Chiesi, Essex/Schering-Plough, GSK, Janssen-Cilag, Leti, MEDA, Merck, MSD, Mundipharma, Novartis, Nycomed/Takeda, Pfizer, Revotar, Roche, Sanofi-Aventis, Sandoz-Hexal, Stallergens, TEVA, UCB, and Zydus/Cadila. He has also received research funding from GSK and MSD.

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