Year-in-Review

Adult asthma and airway disease

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This review introduces the key articles about adult asthma published in 2016.

Tools to help in asthma management

Studies on risk factors for worse outcomes in adult asthma were reported, including depression, hypertension, chronic sinusitis, female sex, obesity, and beta receptor polymorphisms. A cross-sectional study of 20,271 adults using the 2007-2012 National Health and Nutrition Examination Survey reported that depressive symptoms were associated both significantly and linearly with asthma and independent of anxiety and other potential confounders.[1] Importantly, among asthmatics, bronchodilator response was significantly reduced in those with major depression. In a retrospective case-control analysis of almost 120,000 adult asthmatics evaluated in a large health maintenance organization, compared with controls without hypertension, those asthmatics with hypertension displayed evidence in multivariable analyses of enhanced asthma morbidity, including excessive rescue bronchodilator use, asthma ED visits or hospitalizations, and OCS dispensed.[2] In a large US farming population, early-life farm exposures, particularly maternal farming activities while pregnant, were strongly associated with reduced risk of atopy in adults.[3] The Pregnancy Asthma Control Test, a modified version of the Asthma Control Test (ACT), was validated by telephone in 159 pregnant asthmatics, and now can be used clinically to monitor these patients.[4] Lung sound analysis, a simple, noninvasive, and reproducible technique, was shown to correlate with airway inflammation and bronchodilator responsiveness in 31 adults with mild-tomoderate asthma.[5]

Risks for acute exacerbation

In a population-based cohort study, most patients with incident severe asthma used fewer resources over

time, indicating a long-term transition to milder asthma. Potentially modifiable risk factors for poor prognosis of severe asthma include low socioeconomic status and high comorbidity burden.[6] A multicenter, prospective study of patients with severe, life-threatening asthma demonstrated that significant heterogeneity exists among patients with severe or life-threatening asthma exacerbation. Differences were observed in the severity of asthma symptoms and use of inhaled corticosteroids at baseline, and the presence of comorbid COPD.[7] Among a national representative sample of 4.3 million ED visits for asthma exacerbations, sex differences were reported in the frequency of hospitalizations.[8] Females among young children aged 4 to 11 years and adults 18 to 64 years evidenced increased risk for hospitalization, whereas the reverse was seen for females 12 to 17 years of age, after adjusting for confounders. Compared with patients with persistent asthma only, patients with persistent asthma and a COPD diagnosis exhibited significantly more comorbidities (gastroesophageal reflux disease, pneumonia, chronic sinusitis, and nasal polyposis), more indices for uncontrolled asthma based on impairment and risk, and concomitant higher intensity of asthma treatment. In addition, elevated blood eosinophil levels in patients with persistent asthma and a COPD diagnosis were an independent risk factor for future asthma exacerbations, suggesting a common inflammatory component between patients with persistent asthma with or without a COPD diagnosis.[9]

Disease burden of asthma

A study conducted in 101 health centers throughout Spain over 12 months revealed that greater frequency of symptoms and more severe AR are associated with higher costs. Indirect costs are almost threefold direct costs, especially in presenteeism.[10] The increase in disease burden associated with obesity might be explained, in part, by the corticosteroid pharmacokinetic abnormalities reported in obese and overweight corticosteroidresistant asthmatics.[11] In a real-world managed-care setting, the clinical and economic burden of the 2.3% of patients with severe uncontrolled asthma was determined among a cohort of 25,935 adolescents and adults with persistent asthma.33 During a year of follow-up in this retrospective study, severe uncontrolled patients, despite high-dose controller therapy, exhibited significantly more asthma exacerbations, excessive short-acting b2-agonist (SABA) use, and higher all-cause and asthma-related costs than patients with nonsevere uncontrolled asthma.[12] The disease burden of adult patients with persistent asthma who also are diagnosed with chronic obstructive pulmonary disease (COPD) was also reported using a large retrospective administrative database.[13] In one real-life investigation study, ACOS was prevalent in the general population, and it affected to a large extent females with less smoking exposure compared with patients with COPD only. Cardiovascular comorbidities in particular contributed most to overall hospitalization risk of patients with ACOS.[14]

Genetic polymorphisms in phenotyping patients with asthma

WGCNA constructed 64 gene network modules, including modules corresponding to T1 and T2 inflammation, neuronal function, cilia, epithelial growth and repair mechanisms and genes in modules linked to epithelial growth and repair (EGR) and neuronal function were markedly decreased in SA.[15] Transcriptomics profiles generated by microarray analysis of blood from 610 asthmatic and control participants in U-BIOPRED identified that blood gene expression differences between clinically defined subgroups of asthmatics and non-asthmatic individuals.[16] Combining GWAS with subsequent lung eQTL analysis revealed disease-associated SNPs regulating lung mRNA expression levels of potential new asthma genes. Adding BHR to the asthma definition does not lead to an overall larger genetic effect size than analysing (doctor's diagnosed) asthma.[17] Homozygosity for the Arg/Arg polymorphism of the adrenergic beta-2 receptor was reported to be associated with the severity of allergic asthma, comparing a cohort with severe to mild-to-moderate asthma based on Global Initiative for Asthma step-care needed for asthma control.[18]

Treatment of asthma

Asthma treatment was highlighted in several 2016 Journal articles. There was a study demonstrating the efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β2-agonists.[19] and it provided support for benralizumab to be an additional option to treat this disease in this patient population. A randomized sham controlled 40-week study of 247 adults and children with controlled persistent asthma reported that comprehensive individualized household allergen avoidance intervention significantly reduced all measured allergen levels of cat, dog, and dust mite in the bedroom and cockroach and mouse in the kitchen and bedroom.[20] Unfortunately, there was no significant reduction in the NAEPP-based step-care level, emphasizing the challenges in improving asthma outcomes with environmental intervention. The long-acting antimuscarinic agent tiotropium received FDA approval for the treatment of asthma in September 2015. A double-blind, placebo-controlled phase III 12-week dose ranging study demonstrated the bronchodilator efficacy, safety, and tolerability of tiotropium at once daily dosage of 2.5 mcg and 5 mcg delivered as Respimat as add-on therapy to low- to mediumdose ICS in adults with uncontrolled asthma.[21] Both dosages significantly increased forced expiratory volume in 1 second and peak flow rates compared with placebo, extending the documentation of the benefit of tiotropium to uncontrolled adult asthmatics on low- to medium-dose ICS. In a post hoc analysis of lung function during a 12-week clinical trial of 386 patients with moderate-to-severe asthma receiving either a combination ICS/long-acting b2-agonist (LABA), monotherapy ICS, monotherapy LABA, or placebo budesonide, fixed airway obstruction was found to be persistent in 29%, inconsistent in 31%, and not fixed in 40%.[22] Study withdrawal due to predefined adverse asthma events was more frequent in patients with

persistent or inconsistent fixed airway obstruction.

IgE and Omalizumab

Omalizumab, an anti-IgE, has served as a valuable biologic for the treatment of moderate-to-severe uncontrolled asthma despite high-dose conventional controller medication in adults and children. Omalizumab therapy of non-atopic asthmatics reduces bronchial mucosal IgE+ mast cells and improves lung function despite withdrawal of conventional therapy.[23] Determining candidacy for and dosing of omalizumab therapy is based on the serum level of total IgE. Hatipoglu et al[24] reported variability of serum IgE when measured every 2 months in 17 moderate-severe adults with allergic asthma. The probability of experiencing at least a 10% change was 69%, and clinical decisions in determining candidacy for treatment or dosing would have been affected by IgE variability in 7 of 17 (41%) patients. More recently, exacerbations of ABPA while on omalizumab therapy in 3 patients were associated with at least doubling of total serum IgE levels,[25] and in another case report, effectiveness following omalizumab therapy for ABPA was accompanied by a substantial reduction of total serum IgE.[26] These findings support monitoring serum IgE during omalizumab treatment of ABPA, although larger confirmative studies are needed.

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