A SELECTION OF TEN READINGS ON TOPICS RELATED TO "WHAT'S NEW IN ASTHMA MANAGEMENT"

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Selection of readings made by A/Prof Goh Lee Gan

READING I. 2020 ERS/ATS GUIDELINE FOR SEVERE ASTHMA MANAGEMENT

Holguin F(1)(2), Cardet JC(3), Chung KF(4), et al (34 authors). Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline. Eur Respir J. 2020 Jan 2;55(1):1900588. PMID: 31558662.

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(4)Experimental Studies Medicine, National Heart and Lung Institute, Imperial College London, London, UK, et al (34 authors).

ABSTRACT

This document provides clinical recommendations for the management of severe asthma. Comprehensive evidence syntheses, including meta-analyses, were performed to summarise all available evidence relevant to the European Respiratory Society/American Thoracic Society Task Force's questions. The evidence was appraised using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach and the results were summarised in evidence profiles. The evidence syntheses were discussed and recommendations formulated by a multidisciplinary Task Force of asthma experts, who made specific recommendations on six specific questions.

After considering the balance of desirable and undesirable consequences, quality of evidence, feasibility, and acceptability of various interventions, the Task Force made the following recommendations: 1) suggest using anti-interleukin (IL)-5 and anti-IL-5 receptor α for severe uncontrolled adult eosinophilic asthma phenotypes; 2) suggest using a blood eosinophil cut-point $\geq 150 \mu$ L-1 to guide anti-IL-5 initiation in adult patients with severe asthma; 3) suggest considering specific eosinophil ($\geq 260 \mu$ L-1) and exhaled nitric oxide fraction ($\geq 19.5 \text{ ppb}$) cut-offs to identify adolescents or adults with the greatest likelihood of response to anti-IgE therapy; 4) suggest using inhaled tiotropium for adolescents and adults with severe uncontrolled asthma despite Global Initiative for Asthma (GINA) step 4-5 or National Asthma Education and Prevention Program (NAEPP) step 5 therapies; 5) suggest a trial of chronic macrolide therapy to reduce asthma exacerbations in persistently symptomatic or uncontrolled patients on GINA step 5 or NAEPP step 5 therapies, irrespective of asthma phenotype; and 6) suggest using anti-IL-4/13 for adult patients with severe eosinophilic asthma and for those with severe corticosteroid-dependent asthma regardless of blood eosinophil levels. These recommendations should be reconsidered as new evidence becomes available.

READING 2. CHARACTERISATION OF SEVERE ASTHMA WORLDWIDE

Wang E(I), Wechsler ME(2), Tran TN(3), et al (26 authors). Characterisation of Severe Asthma Worldwide: Data From the International Severe Asthma Registry. Chest. 2020 Apr;157(4):790-804. PMID: 31785254.

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BACKGROUND: Clinical characteristics of the international population with severe asthma are unknown. Intercountry comparisons are hindered by variable data collection within regional and national severe asthma registries. We aimed to describe demographic and clinical characteristics of patients treated in severe asthma services in the United States, Europe, and the Asia-Pacific region.

METHODS: The International Severe Asthma Registry retrospectively and prospectively collected data in patients with severe asthma (≥ 18 years old), receiving Global Initiative for Asthma (GINA) Step 5 treatment or with severe asthma remaining uncontrolled at GINA Step 4. Baseline demographic and clinical data were collected from the United States, United Kingdom, South Korea, Italy, and the Severe Asthma Web-based Database registry (including Australia, Singapore, and New Zealand) from December 2014 to December 2017.

RESULTS: We included 4,990 patients. Mean (SD) age was 55.0 (15.9) years, and mean (SD) age at asthma onset was 30.7 (17.7) years. Patients were predominantly female (59.3 percent) and white (72.6 percent), had never smoked (60.5 percent), and were overweight or obese (70.4 percent); 34.9 percent were at GINA Step 5; and 57.2 percent had poorly controlled disease. A total of 51.1 percent of patients were receiving regular intermittent oral corticosteroids, and 25.4 percent were receiving biologics (72.6 percent for those at GINA Step 5). Mean (SD) exacerbation rate was 1.7 (2.7) per year. Intercountry variation was observed in clinical characteristics, prescribed treatments, and biomarker profiles.

CONCLUSIONS: Using a common data set and definitions, this study describes severe asthma characteristics of a large patient cohort included in multiple severe asthma registries and identifies country differences. Whether these are related to underlying epidemiological factors, environmental factors, phenotypes, asthma management systems, treatment access, and/or cultural factors requires further study.

READING 3. ADD-ON THERAPIES IN PRIMARY CARE ASTHMA MANAGEMENT

Kaplan A(I), FitzGerald JM(2), Buhl R(3), et al (5 authors). Comparing LAMA with LABA and LTRA as addon therapies in primary care asthma management. NPJ Prim Care Respir Med. 2020 Nov 11;30(1):50. PMID: 33177503.

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ABSTRACT

The Global Initiative for Asthma recommends a stepwise approach to adjust asthma treatment to the needs of individual patients; inhaled corticosteroids (ICS) remain the core pharmacological treatment. However, many patients remain poorly controlled, and evidence-based algorithms to decide on the best order and rationale for add-on therapies are lacking.

We explore the challenges of asthma management in primary care and review outcomes from randomised controlled trials and meta-analyses comparing the long-acting muscarinic antagonist (LAMA) tiotropium with long-acting β 2-agonists (LABAs) or leukotriene receptor antagonists (LTRAs) as add-on to ICS in patients with asthma.

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In adults, LAMAs and LABAs provide a greater improvement in lung function than LTRAs as add-on to ICS. In children, results were positive and comparable between therapies, but data are scarce. This information could aid decision-making in primary care, supporting the use of add-on therapy to ICS to help improve lung function, control asthma symptoms and prevent exacerbations.

READING 4. ASTHMA ACROSS AGE: INSIGHTS FROM PRIMARY CARE

Kaplan A(I), Hardjojo A(2), Yu S(2), et al, (4 authors). Asthma Across Age: Insights From Primary Care. Front Pediatr. 2019 May 3;7:162. PMID: 31131265

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ABSTRACT

Asthma is a heterogeneous disease comprising of multiple phenotypes and affects patients from childhood up to old age. In this review, we summarise the current knowledge on the similarities and differences in asthma across different age-groups, with emphasis on the perspective from primary care.

Despite the similar disease presentation, phenotyping studies showed that there are differences in the distribution of phenotypes of asthma presenting in childhood compared to that in adulthood. Whereas, asthma with early age of onset tends to be of the atopic phenotype, the disease shifts toward the non-atopic phenotypes at later ages.

Studies within primary care patients aiming to elucidate risk factors for future asthma exacerbation have shown pediatric and elderly patients to be at higher risk for future asthma attacks compared to other adult patients. Regardless, both pediatric and adult studies demonstrated previous asthma episodes and severity, along with high blood eosinophil to predict subsequent asthma attacks. Differences in childhood and adult asthma are not limited to the underlying phenotypes but also extends to the challenges in the diagnosis, treatment, and management of the disease. Diagnosis of asthma is complicated by age-specific differential diagnoses such as infectious wheezing and nasal obstruction in children, and aging-related problems such as heart disease and obesity in the elderly. There are also age-related issues leading to decreased disease control such as non-adherence, tobacco use, difficulty in using inhalers and corticosteroid-related side effects which hinder asthma control at different patient age-groups.

Several clinical guidelines are available to guide the diagnosis and drug prescription of asthma in pediatric patients. However, there are conflicting recommendations for the diagnostic tools and treatment for pediatric patients, posing additional challenges for primary care physicians in working with multiple guidelines. While tools such as spirometry and peak flow variability are often available in primary care, their usage in preschool patients is not consistently recommended. FeNO measurement may be a valuable non-invasive tool which can be adopted by primary physicians to assist asthma diagnosis in preschool-age patients.

READING 5. NIPPLE SHADOW CAN BE A CONFOUNDING CXR PULMONARY NODULE

Boo WH(1), Chan YC(2). Lo, the ever confounding nipple shadow! Malays Fam Physician. 2020 Nov 10;15(3):79-82. eCollection 2020. PMID: 33329866

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ABSTRACT

The discovery of a solitary pulmonary nodule (SPN) on chest imaging can be alarming for both the clinician and the patient. In the absence of a uniform guideline, managing SPN is nothing short of challenging for primary care physicians (PCPs). We present a case here of a patient presenting with prolonged cough who also displayed unilateral SPN on her chest radiograph. Through further examination, this presence was later shown to be a nipple shadow simulating SPN, and the patient was spared unnecessary testing and psychological distress.

READING 6. SUBSOLID PULMONARY NODULE ON CT IMAGING

Azour L(1), Ko JP(2), Naidich DP(2), et al (4 authors). Shades of Gray: Subsolid Nodule Considerations and Management. Chest. 2021 May;159(5):2072-2089. PMID: 33031828.

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ABSTRACT

Subsolid nodules are common on chest CT imaging and may be either benign or malignant. Their varied features and broad differential diagnoses present management challenges. Although subsolid nodules often represent lung adenocarcinomas, other possibilities are common and influence management. Practice guidelines exist for subsolid nodule management for both incidentally and screening-detected nodules, incorporating patient and nodule characteristics. This review highlights the similarities and differences among these algorithms, with the intent of providing a resource for comparison and aid in choosing management options.

READING 7. PERIPHERAL LUNG NODULE ON CXR AND CHEST CT SCANS

Khan T(I), Usman Y(I), Abdo T(I), et al (6 authors). Diagnosis and management of peripheral lung nodule. Ann Transl Med. 2019 Aug;7(15):348. PMID: 31516894.

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ABSTRACT

A solitary pulmonary nodule (SPN) is a well-defined radiographic opacity up to 3 cm in diameter that is surrounded by unaltered aerated lung. Frequently, it is an incidental finding on chest radiographs and chest CT scans.

Determining the probability of malignancy is the first step in the evaluation of SPN. This can be done by looking at specific risk factors and the rate of radiographic progression. Subsequent management is guided by the type of the nodule. Patients with solid nodules and low pretest probability can be followed radiographically; those with high probability, who are good surgical candidates, can be referred for surgical resection. When the pretest probability is in the intermediate range additional testing such as biopsy should be done. Various modalities are now available to obtain tissue diagnosis. These modalities differ in their yieldand complication rate.

Patients with SPN should be well informed of each approach's risks and benefits and should be able to make an informed decision regarding the different diagnostic and therapeutic modalities.

READING 8. PATIENTS' EXPERIENCE OF SEVERE ASTHMA ADD-ON PHARMACOTHERAPIES

Clark VL(1)(2), Gibson PG(1)(3), McDonald VM(1)(2)(3). The Patients' Experience of Severe Asthma Add-On Pharmacotherapies: A Qualitative Descriptive Study. J Asthma Allergy. 2021 Mar 15;14:245-258. PMID: 33758515.

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ABSTRACT

PURPOSE: Add-on therapies for severe asthma are continually emerging with proven efficacy in randomised controlled trials. To date, however, there are no qualitative studies exploring patients' experiences with these treatments. We aimed to understand the experience of patients who were treated with an add-on therapy for their severe asthma.

PATIENTS AND METHODS: A qualitative descriptive study was conducted, participants were recruited from the respiratory clinics and databases of a tertiary referral hospital. Participants with treatment-refractory severe asthma (n=20) prescribed an add-on therapy for >4 months (75 percent mepolizumab; 25 percent omalizumab, and 25 percent macrolide) were recruited. Qualitative semi-structured interviews were conducted, with interviews thematically analysed.

RESULTS: Participants' mean (SD) age was 59.5 (15.3) years, and 50 percent were male. Participants reported 4.5 (2.3) exacerbations in the past year. Asthma Control Questionnaire score was 2.0 (1.4). The monoclonal add-on therapies had been prescribed for a median (IQR) of 12.5 (7.0, 24.0) months. Experience was captured in four emergent themes: "Life is just easier" provided an overall message that the add-on therapy made the participants' life easier in terms of increasing participation, levelling out symptoms, providing more energy and reducing healthcare use. "Prednisone: A necessary evil" was discussed, particularly in terms of dose and dependence and damaging side effects. The theme "worry and hope for the future" referenced treatment non-response or cessation of effect which was discussed by some participants. Finally, "holistic care" was centred on the sentiment that the participant's asthma management and overall health were not related to one aspect or medication alone.

CONCLUSION: Patients with severe asthma experience vast improvements in quality-of-life and life participation with add-on therapies, but there remains a significant burden related to oral corticosteroids and incomplete treatment responses. Addressing this residual burden is an important area for future research.

READING 9. YOGA AND MINDFULNESS ACTIVITY HELP HRQOL IN SEVERE ASTHMA

Hiles SA(1), Urroz PD(1), Gibson PG(1)(2), Bogdanovs A(3) et al (5 authors). A feasibility randomised controlled trial of Novel Activity Management in severe ASthma-Tailored Exercise (NAMASTE): yoga and mindfulness. BMC Pulm Med. 2021 Feb 27;21(1):71. PMID: 33639922.

doi: 10.1186/s12890-021-01436-3 [Free full text].

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BACKGROUND: Physical inactivity is common in severe asthma and associated with poor health outcomes. New approaches are needed to address physical inactivity in this group.

OBJECTIVE: To examine whether yoga and mindfulness improves health-related quality of life (HRQoL) compared with a minimal active control group and collect feasibility data to inform future studies.

METHODS: Over 12-weeks, adults with severe asthma were recruited. Participants were randomised 2:1 to parallel yoga or control groups. All participants received an activity tracker. The yoga group received tailored group classes twice a week for 16-weeks with a qualified yoga instructor. The control group set activity goals with a research officer and received eight progress calls. Outcomes were assessed at 16-weeks. Primary outcome was St George's Respiratory Questionnaire (SGRQ). Secondary outcomes included asthma control, physical activity, breathlessness, and inflammation. Face-to-face qualitative interviews were conducted to determine acceptability.

RESULTS: There were 15 participants randomised to yoga (mean 67 years; 60 percent female) and 9 to control (68 years; 56 percent female). Planned comparisons indicated the yoga group had greater SGRQ improvement than the control group. There was little change in secondary outcomes. Moderate-vigorous activity increased substantially in the control group. Participants found the intervention acceptable; key barriers and facilitators were social connection, the setting, addressing breathing and asthma symptoms, changing their mindset, and the intersection of different elements.

CONCLUSION: A yoga and mindfulness intervention was feasible, acceptable to patients and improved HRQoL. The findings will inform design of much needed future research into physical activity interventions for severe asthma.

READING 10. CHALLENGES FACED IN ADULT ASTHMA

Dhar R(I), Ip M(2), Kulkarni T(I), et al (8 authors). Challenges faced in managing adult asthma: A perspective from Asian countries. Respirology. 2020 Dec;25(I2):I235-I242. PMID: 32885896

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ABSTRACT

Asthma imposes a significant burden on the health system and patients' quality of life. Within Asia, there is large variability in several cultural, social and economic factors ultimately influencing the management of asthma. Differences in risk factors and asthma management practices across Asia make asthma a truly 'mixed-bag' phenomenon. With the advent of biological agents and the consequent emphasis on asthma phenotyping and endotyping, it is more important than ever to understand the diverse nature of asthma as a disease. This is a collaborative review within Asia to highlight the differences in management of adult asthma, and the local modifications that are made to international guidelines. This review paves the way for a future Asian collaborative network in asthma epidemiological research.