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ACUTE ASTHMA, PROGNOSIS, DIAGNOSIS AND TREATMENT

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Abstract

Background: Asthma is a chronic airway inflammatory disease associated with the variable expiratory flow, variable respiratory symptoms, and exacerbations, which sometimes require hospitalization or may be fatal. It is not only patients with severe and poorly controlled asthma that are at risk for a severe acute exacerbation, but this has also been observed in patients with otherwise mild or moderate asthma. This review discusses the prevalence, pathophysiology, prognosis, diagnosis, and current management protocols of acute asthma exacerbations. A web-based search utilizing the advanced characteristics of different databases like PubMed, Google Scholar, Embase, Scopus, and Cochrane electronic databases was carried out.
Keywords: Acute, Asthma, Exacerbations, Prognosis, Diagnosis, Management.

Introduction:

Asthma is described as a chronic inflammatory disorder of the airways. Chronic inflammation is correlated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and/or coughing that can vary over time and in intensity [1].

Symptom episodes are commonly correlated with broad but changeable airflow obstruction within the lungs that is frequently reversible either spontaneously or with suitable asthma therapy, such as a fast-acting bronchodilator [1].

According to the 2014 British Guidelines for Asthma, severe acute asthma is described as the asthma exacerbation that performs with any of the following: PEF 33–50% best or predicted, respiratory rate ≥ 25/min, heart rate ≥ 110/min, and inability to complete sentences in one breathe [2].

About asthma, an exacerbation is defined as an event characterized by a change from the case's prior status, including a progressive improvement in relevant symptoms and a decrease in respiratory function [3]. The latter can be quantified by respiratory function measures such as peak expiratory flow (PEF) and forced expiratory volume in 1 s (FEV1), which when associated with the case's past or expected values, show the decline in expiratory airflow, the prominent pathophysiological impact of an asthma strike [3]. The most frequent conditions of these exacerbations are exposure to external factors, like indoor and outdoor allergens [3], air pollutants [4], and respiratory tract infections (primarily viral mainly human rhinovirus (HRV) [5]. This review discusses the prevalence, pathophysiology, diagnosis, and current management protocols of acute asthma exacerbations.

Materials and Methods:

A web-based search utilizing the advanced characteristics of different databases like PubMed, Google Scholar, Embase, Scopus, and Cochrane electronic databases was carried out. The major MeSH and other keywords like; Acute asthma definitions, prevalence of acute asthma, diagnosis, and management of acute asthma, etc., were used to search the databases. The search included the latest studies published from 2010 to 2020, and the search was limited to studies published in English.

Prevalence of asthma and acute asthma:

The prevalence of asthma is variable worldwide, ranging from 1-20% for both children and adults [6]. These wide variations are related to environmental variations among

countries and the use of different measurement tools and different epidemiological definitions of asthma. In Saudi Arabia, the prevalence of asthma in children and adolescents has been investigated. According to the Saudi Initiative for Asthma (SINA 2016), the overall prevalence of asthma in children ranges from 8-25%, based on studies conducted over the past three decades [7]. Results from a national Saudi household survey in 2013, estimating the burden of chronic medical conditions, including asthma among the Saudi population aged 15 years or older, indicated a self-reported clinical diagnosis of asthma to be 4.05% [8]. The asthma prevalence in Saudi adults is under-investigated. Globally no accurate figures describe the rate of acute asthma, but there are sufficient data regarding asthma-related hospitalizations and asthma-related death. Current studies assess the risk of death of the hospitalized cases due to asthma exacerbation as less than 0.5% [9].

Pathophysiology:

Asthma is correlated with T helper cell type-2 (Th2) immune responses typical of other atopic diseases. Asthma triggers may involve allergic (e.g., home dust mites, cockroach debris, animal dander, pollens, and mold) and non-allergic (e.g., viral infections, tobacco smoke, exercise, and cold air) stimuli, which create a cascade of effects causing chronic airway infection. Raised Th2 cells in the airways release specific cytokines, including interleukin (IL)-4, IL-5, IL-9, and IL-13, and promote eosinophilic inflammation immunoglobulin E (IgE) formation. IgE production, in turn, triggers the liberation of inflammatory mediators, such as histamine and cysteinyl leukotrienes, that cause bronchospasm (a contraction of airways smooth muscle), edema, and raised mucous secretion, which causes the characteristic symptoms of asthma [10].

The pathophysiology of acute asthma is less obvious due to poor knowledge. This is because of the difficulty in explaining disease pathology and getting samples through the attack. The pathological indications frequently rely on the trigger. At least 80% of cases of moderate-to-severe acute asthma are triggered not only by viruses, most commonly rhinovirus but also by respiratory syncytial and influenza viruses [11]. Viral infections can cause significant epithelial damage, and symptoms tend to be more severe and last longer. On the other hand, allergen- or irritant-triggered attacks tend to be milder and resolve more quickly. Recurrent attacks may lead to a progressive decline in lung function and increasing baseline asthma severity [12].

Symptoms:

Symptoms of acute asthma include chest tightness, cough (with or without sputum), the sensation of air hunger, the ability to lie flat, insomnia, and severe fatigue. The marks of severe asthma involve accessory muscles of respiration, hyperinflation of the chest, diaphoresis, tachycardia, tachypnea, obtundation, wheezing, anxious look, inability to make sentences, and problem in lying down. Altered mental status, without or with cyanosis, is an ominous symptom, and urgent emergency care and hospitalization are needed [13]. A detailed investigation should include examining for signs and symptoms of pneumonia, pneumothorax, or a pneumomediastinum, the latter of which can be investigated using palpation for subcutaneous crepitations, particularly in the supraclavicular areas of the chest wall [14]. Particular consideration must be given to the case's blood pressure, pulse, and respiratory rate. Tachycardia and tachypnea might be suggestive of a moderate-to-severe exacerbation, whereas bradycardia might indicate impending respiratory arrest. Pulsusparadoxus is often present and might correlate with the severity of exacerbation [14].

Diagnosis

Harm from asthma medications may arise from misdiagnosis [15]. Hence, a comprehensive workup is important to ascertain whether the patient has severe asthma [16].

- **Patient history**

A detailed history is the first step to the assessment and diagnosis [16]. The medical history should focus on characterizing the specific symptoms, frequency, and severity [17]. Clarification of the onset of symptoms, determination of the severity of exacerbations, and associated comorbidities are also essentials [16]. Accordingly, clinical questionnaires can facilitate these assessments [16]. When critical information of the patient's symptoms is gathered, clinicians gain a better understanding of the patient's problem. The most frequent abnormal physical outcomes are an extended expiratory phase and wheezing on auscultation, which confirms the presence of airflow limitation [1]. Physical examination of the cardio-respiratory system is also necessary [16].

- **Objective measures to prove variable expiratory airflow limitation**.

There are several standard assessments included in lung function examinations in asthma. These involve but are not limited to estimating airflow limitation within spirometry and peak expiratory flow.

- **Spirometry**

Spirometry measures airflow parameters like the forced vital capacity (FVC) and the forced expiratory volume in 1 s (FEV1). Lung volumes are not estimated with spirometry and rather need full pulmonary function testing. The ratio of FEV1 to FVC presents an estimate of airflow obstruction. In the public population, the FEV1/FVC ratio is usually greater than 0.75–0.80 in adults and 0.90 in infants. Any amounts less than these recommend airflow limitation and enhance a diagnosis of asthma [1, 17].

- **Peak expiratory flow (PEF)**

Peak expiratory flow (PEF) monitoring is an adequate alternative when spirometry is impossible and can help

diagnose occupational asthma and/or monitor response to asthma treatments. But, PEF is not suggested for diagnosing asthma in infants. PEF is often estimated in the morning and the evening. A diurnal difference in PEF of more than 20% or an enhancement of at least 60 L/min or at least 20% following the breathing of a rapid-acting bronchodilator recommends asthma [18].

- **Non-invasive markers of airway inflammation**

The determination of inflammatory markers such as sputum eosinophilia or exhaled nitric oxide can also help diagnose asthma. Proof recommends that exhaled nitric oxide levels can assist in diagnosing asthma and may also be useful for monitoring case response to asthma treatment [19].

- **Allergy skin testing**

Allergy skin-prick (epicutaneous) examination is suggested to recognize probable environmental allergic asthma triggers and effectively recognize the asthma phenotype of the case. The examination is done by using the allergens relevant to the case's geographic area. Although allergen-specific IgE examinations supply an in vitro estimation of a cases' certain IgE levels for certain allergens have been recommended as a choice for skin examinations, these tests are less sensitive, more invasive, and more costly than skin prick experiments [1, 18]. There is no particular age at which a skin prick examination can be done.

Treatment

- **Inhaled corticosteroids ICS**

In the event of acute asthma, there is a different approach to their use. Current recommendations suggest that high dose inhaled corticosteroids ICS given within the first hour of the patient's presentation in the emergency department reduce hospital admissions rates for cases not on systemic corticosteroid treatment [1]. Current proof, however, seems to be opposing concerning their appearance without the use of systemic corticosteroids when the rate of hospital admissions or changes in lung function has been studied [20].

- **Oxygen supply**

Patients experiencing an acute severe or life-threatening asthma exacerbation should be referred to the emergency department [21]. Guideline-based emergency evaluation and management of severe asthma exacerbations in adults consists of supplemental oxygen to maintain pulse oximetry at measured oxygen saturation levels of 93% to 95% 2

- **SABAs and SAMAs**

Short-acting β2-agonists (SABAs) and short-acting muscarinic antagonists (SAMAs), and systemic corticosteroids. The method of SABA delivery does not appear to affect outcomes. A Cochrane review reported that among patients presenting with a severe exacerbation, there was no association of treatment with SABA via a nebulizer vs. treatment via MDI and a spacer for the outcome of hospitalization rates after the emergency department [22]. However, the combination of SABA and SAMA bronchodilators was associated with a lower hospitalization rate in adults presenting with a severe asthma exacerbation compared with SABA alone [22]. Chest imaging should be reserved for patients in whom pulmonary consolidation or pneumothorax is suspected [22].

- **Magnesium sulfate**

The role of magnesium sulfate (intra venous or inhaled) as an adjunctive treatment to manage asthma exacerbations has been controversial. Goodacre et al. [23] conducted the largest clinical trial to date on the effect of magnesium sulfate on hospitalization rates in individuals with severe asthma exacerbations. This multicenter, double-blind trial randomized 1109 patients to receive nebulizer magnesium sulfate (MgSO4), intravenous MgSO4, or placebo in addition to standard care. Compared with placebo, intravenous MgSO4was associated with a non-significant decrease in hospital admissions. A subsequent Cochrane meta-analysis [24] that included the Goodacre et al. [23] trial and ten others estimated that intravenous MgSO4was associated with reduced hospital admissions, supporting the use of this treatment in the management of severe acute exacerbations in the emergency care setting. Another Cochrane meta-analysis [25] that also incorporated the Goodacre et al. [23] trial assessed inhaled MgSO4 in individuals with acute asthma and concluded that, while current evidence precludes certainty, inhaled MgSO4 is unlikely to be associated with benefit beyond current standard treatments.

- **Heliox**

Heliox is a mixture of helium (70–80%) and oxygen (20–30%). Heliox has demonstrated the greatest benefit for improving symptoms when used as a nebulizing gas for a beta-2 agonist medication. The benefit is generally seen within minutes after the initiation of therapy [26]. Another study has demonstrated that using heliox as a carrier gas improves gas delivery up to 50% in a mechanical model for MDIs and nebulizers [27].

- **Antibiotics**

There is no evidence supporting the antibiotic use per se for severe acute asthma unless the patient's history and clinical assessment indicate infection. In a retrospective cohort study, it has been reported that, in cases hospitalized with acute asthma and getting OCS, antibiotic use was correlated with longer hospital stay and hospital cost. In contrast, it held a similar risk of treatment failure [28]. In a previous US study, 60% of the cases admitted to hospital with asthma exacerbation obtained antibiotics, with no clear evidence accompanying this decision [29]. Modern guidelines recommend against their practice and that they should be recognized after optimizing other management choices and when there is obvious infection evidence [1].

Conclusion

Acute severe asthma is described as the asthma exacerbation that exhibits any of the following: PEF 33–50% best or prognosticated, respiratory rate ≥ 25/min, heart rate ≥ 110/min, and inability to complete sentences in one breathe. Globally no accurate figures describe the rate of severe acute asthma, but there are sufficient data regarding asthma-related hospitalizations and asthma-related mortality. Symptoms of acute asthma include chest tightness, cough, the sensation of air hunger, the ability to lie flat, insomnia, and severe fatigue. Patient history, lung function examinations in asthma, Non-invasive markers of airway inflammation, and allergy skin testing are the most effective diagnostic tools. The most recent management protocols were inhaled corticosteroids ICS, oxygen supply, Short-acting β2-agonists (SABAs) and short-acting muscarinic antagonists (SAMAs), systemic corticosteroids, magnesium sulfate, heliox, and antibiotics.

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