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Review Article

Causes, diagnosis and treatment of occupational asthma

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ABSTRACT

Occupational asthma is usually characterized by airway hyperresponsiveness, airway obstruction, and airway inflammation that usually result from exposure to specific irritants in the workplace and is not usually associated with any evidence of exacerbation outside the workplace. Occupational asthma can be associated with complicated long-term outcomes because affected patients are not usually aware of the hazards of the condition. Therefore, applying adequate diagnostic and management approaches is essential to enhance the outcomes among high-risk workers. In the present literature review, we have discussed the causes, diagnosis, and management of occupational asthma based on the evidence obtained from the current studies in the literature. Our findings indicated the presence of various environmental triggers that can lead to the development of asthma in the workplace, including HMW and LMW compounds. The diagnosis of asthma is based on obtaining a thorough personal and clinical history from the affected patient. However, such approaches have been reported to have low specificity rates, and therefore, the diagnosis should be established by other measures as lung function tests. The management of asthma is hugely dependent on the clinical phenotypes of occupational asthma. Nevertheless, applying adequate interventions can significantly enhance the outcomes in the affected patients, in addition to the other measures that have been adequately discussed in the manuscript.

Keywords: Occupational asthma, Etiology, Diagnosis, Treatment

INTRODUCTION

Worldwide estimates show that asthma affects around 360 million patients, and it has been demonstrated that work-related asthma represents around a quarter of all of the reported adult-onset asthma.[1,2] Work-related asthma is a term used to describe a certain type of asthma that is associated with the workplace of the affected patients and includes work-exacerbated asthma, and occupational asthma.

Occupational asthma is usually characterized by airway hyperresponsiveness, airway obstruction, and airway inflammation that usually result from exposure to specific irritants in the workplace and is not usually associated with any evidence of exacerbation outside the workplace.[3-5] There are two main clinical phenotypes of asthma that

were reported among the different studies in the literature, including (1) occupational asthma due to exposure to workplace sensitizers and can be immunological or allergic; and (2) occupational asthma due to exposure to irritants at the workplace and is not immunological or allergic but can induce a significant airway reaction that usually leads to the development of reactive airways dysfunction syndrome. Occupational asthma can be associated with complicated long-term outcomes because affected patients are not usually aware of the hazards of the condition. Therefore, applying adequate diagnostic and management approaches is essential to enhance the outcomes among high-risk workers.

The aim of the study was to discuss the causes, diagnosis, and management of occupational asthma.

METHODS

This literature review was based on an extensive literature search in Medline, Cochrane, and Embase databases which was performed on 3rd September 2021 using the medical subject headings (MeSH) or a combination of all possible related terms. This was followed by the manual search for papers in Google Scholar while the reference lists of the initially included papers. Papers discussing the occupational asthma were screened for relevant information, with no limitation placed on date, language, age of participants, or publication type.

DISCUSSION

Causes

Many causative agents can attribute to the development of occupational asthma that has been priorly discussed in the literature, including various airborne agents.[4,6] Estimates show that occupational asthma can occur secondary to the exposure of more than 350 agents.[2,7] Besides, further agents are also being identified each year. The causative agents might be high or low-molecular-weight agents (HMW and LMW). Diisocyanates (an LMW compound that is widely available in glues, various paints, and insulations) and flour (an HMW agent) have been reported to be the most common agents to induce occupational asthma, with an estimated rate of 20% in the developed countries.[8,9]

Fumes, irritant gases, aerosols, and smoke can also lead to the development of occupational asthma. It is well known that HMW agents are usually derived from a plant origin and are composed of polysaccharides and proteins that have a significant ability to induce IgE-related occupational asthma as a result of their complete sensitizing impact.[2] Therefore, the pathology of occupational asthma requires frequent and prolonged exposure to these substances to finally lead to mast cell activation that can significantly trigger the pathology of the condition. Different occupations are being daily exposed to certain HMW compounds that can efficiently induce occupational asthma. For instance, farm and laboratory animal workers can develop asthma secondary to the frequent exposure of mammalian proteins that are usually present in the fur, saliva, dander, and urine.[6,10] Accordingly, it has been demonstrated that having a history of sensitization to animals should be considered a risk factor for developing occupational asthma, although it has been previously demonstrated that general atopy is not usually adequately predictive.

Insects can also have a potential role in developing occupational asthma as they can transfer allergens as indicated with the exposure of bait workers to mealworm larva exoskeleton dust.[11,12] Fish and shellfish, cereals and flours, and exposure to natural rubber latex are also important factors that can contribute to the development of occupational asthma.[6] Natural rubber latex was reported to commonly cause occupational asthma. However, the prevalence of the condition has been significantly reduced as a result of the reduced utilization of latex-powdered gloves. Enzymes are also reported as causative agents and are usually found in multiple occupations as baking, pharmacological preparations, and detergent manufacture.[6,8,13] Many LMW compounds were also reported in the literature to cause occupational asthma, including trimellitic anhydride, diisocyanates, and formaldehyde. These compounds lead to the development of occupational asthma by non-immunological mechanisms. Wood dust can also lead to the development of occupational asthma. Exposure to acrylates and persulfate salts were also reported to cause the condition among dentists and hairdressers, respectively.[6,14-17] Metalloids and metals have also been reportedly associated with occupational asthma. However, the mechanism of such events is poorly understood. The development of occupational asthma can be secondary to exposure to a single compound. Furthermore, it has been demonstrated that certain occupations can expose workers to multiple HMW and LMW substances.

Diagnosis

Early diagnosis of occupational asthma is necessary to enhance the health-related outcomes of the affected patients. The best diagnostic approach can be obtained by a combination of obtaining an adequate clinical and personal history from the patient, and performing indicative diagnostic tests to establish a proper diagnosis. Peak expiratory flow (PEF) can be performed to discover whether any airway changes can be related to the work, sputum eosinophilic counts, non-specific BHR, evidence for Specific sensitization (SPT) and/or FeNO, SIC, sIgE, and Basaltic activation test (BAT).[18] Moreover, it is also recommended that an adequate differential diagnosis should be considered and conditions that might result secondary to the exposure of irritants should be excluded and might include hyperventilation syndrome, vocal cord dysfunction, and mass psychogenic conditions.[19,20] Obtaining a personal history from the patient can be simply guided by asking the patient about the timing of symptoms

worsening, which is usually during the time of work while outside the workplace; symptoms usually relieve. However, it should be noted that asthma symptoms can also be present outside the workplace as a result of the potential exposure to other irritants as smoke, fumes, and performing exercises that might trigger asthma symptoms.[19]

The diagnosis of occupational asthma is usually delayed to 2-3 years following the appearance of symptoms because workers are not usually aware of the condition because potential symptoms remission within the weekends and in the evening tend to fade away when these workers have continuously been exposed to the causative agents.[20] Occupation, respiratory symptoms, the presence of dermatitis or urticaria, and other respiratory conditions as conjunctivitis and/or rhinitis.[19,20] However, it should be noted that obtaining a personal and clinical history is not always adequate to establish a proper diagnosis, and therefore, the diagnosis should be indicated using lung function tests.[19,21,22]

The presence of asthma can be adequately diagnosed by reversible airflow obstruction.[20,23] However, the diagnosis should be conducted when the patient is still employed to conduct a proper comparison of the respiratory functions outside the workplace and while working. However, it was also reported that lung functions tests are not very specific in diagnosing asthma.[24-26] Assessment of the non-specific BHR is considered a mandatory test for patients that suffer from non-irritant conditions. Challenges of histamine and methacholine inhalation have been previously reported to be the most reliable tests for this purpose.[23] Moreover, SIC has also been reported as the gold standard that can adequately indicate the presence of occupational asthma. The mechanism of this test is to mimic the exposure to irritants to trigger occupational asthma-like symptoms similar to what occurs at the workplace.[18]

PEF monitoring was also reported as a valid measure. However, it has low sensitivity when compared to the aforementioned tests.[21,27] Molecular diagnosis and immunological workup have recently been introduced in the literature with many favorable outcomes. Assessment of sIgE by SPT can significantly add to the diagnostic approaches of some phenotypes of occupational asthma that are IgE-mediated and can also identify some of the causative agents, including the HMW and LMW compounds.[19,28,29] Molecular diagnosis can aid in the process of diagnosis. Nevertheless, the main challenge would be to standardize the test to discover the potential allergens. BAT can also be used to discover occupational causative agents, however, many challenges have been reported with these tests as a result of the associated limitations.[30-32] Testing for biomarkers of inflammation can also be another diagnostic tool that might idnicate the presence of occupational asthma. For instance, previous studies demonstrated that the presence of elevated sputum esonophila was a good predictor for diangosing occupational asthma by LMW and HMW agents.[33,34] Applying FeNO in this regard is controversial and further validation of the current evidence is still needed.[20]

Treatment

After the adequate diagnosis of occupational asthma has been established, affected patients should be managed by the same approaches that are applied to non-work-related asthma. Such measures include exposure control to the environmental triggers, asthma education, and the appropriate administration of pharmacological modalities. The latter approach is usually intended to reduce the risk of future events and maximize the benefits of symptoms reduction. Emergency treatment can also be indicated in some cases when the level of exposure is considered excessive. However, it should be noted that applying interventions against exposure to environmental factors would remain the cornerstone in achieving better management regardless of the administered pharmacological modalities.

The management approaches might also differ based on the clinical phenotypes of occupational asthma. Studies indicate that patients with sensitizer-induced asthma should be managed by reallocating them to a different environment.[20] This has been indicated in a previous Cochrane review which indicated that complete removal of exposure was associated with a significant enhancement in lung functions.[35] Besides, another meta-analysis reported that partial removal of exposure was not associated with favorable outcomes as compared to complete avoidance of exposure.[36] However, it should be noted that in cases when the socioeconomic parameters might interfere with re-allocation of the affected patients to another workplace to minimized and eliminate the risk of exposure is not feasible, taking preventions to reduce the risk of exposure is reasonable in such cases to minimize the risk.[20]

Studies have previously demonstrated that adequate application of primary, secondary, and tertiary preventions can significantly reduce the severity and prevalence of sensitizer-induced occupational asthma. Previous studies have also indicated the effectiveness of using respiratory protective equipment,[37] however, these measures should not be considered safe approaches, especially when used on a long-term basis and in patients suffering from severe illnesses.[38] Figure 1 shows the primary, secondary, and tertiary preventive measures that were reported in the literature. Allergen immunotherapy can also be used as an effective pharmacological therapy that can relieve symptoms and enhance outcomes.[39,40] On the other hand, patients suffering from irritant-induced occupational asthma can safely continue their work by applying adequate interventions to minimize the risk of exposure and with adequate asthma control. Oxygen supplementation, administration of corticosteroids, and bronchodialtors inhalation can significantly enhance the outcomes in these patients together with rapidly minimizing the exposure to the irritant when asthma symptoms are triggered.[19-21]

Job modifications, respiratory protective devices, and engineering controls can significantly enhance the environment and reduce the risk of exposure to irritative compounds, which will subsequently reduce the severity of asthma.[41] Education of workers and affected personnel, adequate administration of medical treatment, follow-up programs, and proper application of the prevention measures can effectively reduce the risk and severity of this type of occupational asthma and enhance the outcomes of the affected patients. In this context, affected patients can safely return to their work with no need to discontinue it or change the workplace. Nevertheless, they should be followed up regularly and should be educated to apply adequate interventions to reduce the risk of exposure and stick to their medical treatment to enhance the symptoms and obtain better outcomes.

Prevention	Measures
Primary	• Avoidance of the introduction of new possibles sensitizing agents in the workplace • Using safe alternatives to sensitizing agents • Reduction of the sensitizing potential of agents by chemical or physical process • Education programmes for workers to use safe practices at work • Occupational hygiene measures to reduce exposure to work sensitizers (e.g., use of robotics, containment, ventilation) • Monitoring and controlling exposure levels in the workplace
Secondary (early detection)	• Institute medical-surveillance programs for workers at risk (e.g., periodic respiratory questionnaires, spirometry) • Education of healthcare workers about OA • Education of workers about the risk of OA and to recognize the symptoms of the disease (e.g., workplace or public education programs, information by healthcare provider)
Tertiary (appropiate treatment)	• Evaluation of symptomatic workers to achieve an early and accurate diagnosis • Workers' relocation to reduce the risk of further exposure once the diagnosis is confirmed • Controlling other possible triggers of asthma • Pharmacological treatment to control asthma • Patient's assistance with work-compensation claim to limit socio-economic effects of the diagnosis • Monitoring of the patient's asthma control in future work environment to ensure safe placement.

Figure 1: Primary, secondary, and tertiary interventions for sensitizer-induced occupational asthma.[5,20]

CONCLUSION

The diagnosis of asthma is based on obtaining a thorough personal and clinical history from the affected patient. However, such approaches have been reported to have low specificity rates, and therefore, the diagnosis should be established by other measures as lung function tests. The management of asthma is hugely dependant on the clinical phenotypes of occupational asthma, however, applying adequate interventions can significantly enhance the outcomes in the affected patients, in addition to the other measures that have been adequately discussed in the manuscript.

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