Arch Bronconeumol. 2019;55(7):353–354

Sociedad Española de Neumología y Cirugía Torácica SEPAR

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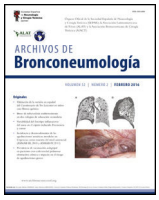

Editorial

Asthma: A New Cardiovascular Risk Factor?☆

Asma: ¿un nuevo factor de riesgo cardiovascular?

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Several epidemiological studies show that asthma, particularly in its uncontrolled eosinophilic phenotype, is a risk factor for developing cardiovascular disease (CVD).[1] A more detailed analysis indicates that women with asthma with disease onset in adulthood and patients with asthma, chronic rhinosinusitis, nasal polyposis, and intolerance to non-steroidal anti-inflammatory drugs are populations with a higher risk of CVD. In this respect, studies have been published in recent years on the association of asthma with CVD,[1–8] some of which looked at retrospective data,[1–4] and several others reported epidemiological prospective cohort studies.[5–8] Two recent meta-analyses made a global evaluation of the results[9,10] and both came to the same two conclusions: (1) the analysis of the data shows an association between asthma and CVD, and (2) this association is particularly clear in women with onset of asthma in adulthood. Another recent study, not included in either of the two meta-analysis, analyzed the relationship between the level of asthma control and the risk of acute myocardial infarction, and found that active asthma, that is, the form that presented persistent clinical signs, exacerbations, and hospital admissions, displays an increased risk, while in clinically stable asthma, the risk of myocardial infarction is similar to that of the non-asthmatic control group.[11]

The mechanism that links both diseases is partially known and includes the predisposition of asthma patients to developing arteriosclerosis and the presence of episodes of acute myocardial ischemia due to vasospasm,[12] even in patients with epicardial arteries with no significant obstruction, a situation in which eosinophilic inflammation plays an important role. The excessive release of cysteinyl leukotrienes, mostly from eosinophils, may contribute to the development of arteriosclerosis and coronary vasospasm. The association between hypereosinophilia and coronary vasospasm has been reported in the literature, especially in patients with eosinophilic granulomatosis with polyangitis, also known as Churg-Strauss vasculitis.[13] The importance of this eosinophilic inflammation is demonstrated by the fact that many of these patients with coronary vasospasm associated with eosinophilic vasculitis or eosinophilic asthma without vasculitis, respond to treatment with systemic glucocorticoids when standard therapy with coronary vasodilators and inhibitors of calcium channels fails.[14] A recent retrospective study investigated the prevalence of asthma in patients with coronary vasospastic angina, and found that the presence of respiratory disease significantly increased the risk of experiencing an episode of vasospastic angina, after adjusting the analysis for other risk factors for developing ischemic heart disease (odds ratio 1.85; 95% CI 1.47–2.32; $p < 0.001$).[12] In another study, Larsen et al.[15] analyzed the characteristics of a series of patients with acute myocardial infarction, and found that patients with myocardial infarction and normal coronary vessels on angiography were younger than those with myocardial infarction and arteriosclerotic coronary stenosis, and had respiratory symptoms typical of obstructive bronchial disease. Rich,[16] motivated by the conclusions of Larsen et al.,[15] noted that 36% of patients in a series with myocardial infarction had a history of obstructive bronchial disease that, in most cases, was diagnosed as asthma. Moreover, patients often also had chronic rhinosinusitis with polyposis, and intolerance to non-steroidal anti-inflammatory drugs. However, some pathology laboratory findings from isolated cases suggest that the coronary vessels may undergo an inflammatory process and remodeling characterized by the presence of abundant eosinophils infiltrating the coronary endothelium, similar to changes seen in the airways of asthma patients. As occurs in asthmatic airways, activated mast cells have also been associated with ischemic coronary vasospasm, and a greater concentration of histamine is observed in coronary blood samples from these patients. Similarly, associations between the severity of ischemia as a result of vasoconstriction and high levels of blood eosinophilia,[17] and the severity of asthma and the intensity of hypereosinophilia in blood and airways have also been detected.

Reducing eosinophilia by treatment with inhaled glucocorticoids has been shown to be effective in the prevention of

☆ Please cite this article as: Picado C, Pernigotti A, Arismendi E. Asma: ¿un nuevo factor de riesgo cardiovascular? Arch Bronconeumol. 2019;55:353–354.

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1579-2129/© 2019 Published by Elsevier España, S.L.U. on behalf of SEPAR.

myocardial infarction in patients with asthma, particularly in those with moderate or severe disease, reducing the risk of a heart attack by 12% for each inhaler cartridge consumed, and by 79% in patients receiving regular continuous treatment with an inhaled glucocorticoid.[18] Treatment with systemic glucocorticoids is also useful in cases in which the acute ischemic vasospastic episode does not respond to conventional treatment. Overall, these observations indicate that achieving good control of persistent asthma must be added to the list of measures usually recommended to prevent CVD.

In short, the data collected from epidemiological studies and clinical observations confirm that asthma, particularly the uncontrolled eosinophilic phenotype, is a risk factor for developing CVD, not only the classic presentation with coronary artery obstruction, but also vasospastic events without obstruction, and this association is more common among women. Eosinophilic inflammation plays a significant role in this association, and its control by treatment with glucocorticoids appears to reduce the risk of developing CVD.

Funding

Integrated Research Program in Asthma, 2016, Spanish Society of Pulmonology and Thoracic Surgery (SEPAR), Spain.

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