The Libyan International Medical University

Faculty of Basic Medical Science

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The Relation Between Hypertension and Asthma

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Abstract :

Asthma and hypertension are common chronic diseases , each with attendant morbidity, mortality, and economic effects.The presence of hypertension with asthma creates an additional health burden; hypertension is the world's most common modifiable risk factor for cardiovascular disease and death. and the prevalence of hypertension, like that of asthma, is increasing, along with costs, morbidity, and mortality Elevated systolic blood pressure was the leading global contributor to preventable death. In the United States, approximately one in three adults has high blood pressure., Patients with asthma are more likely to have hypertension than those who do not, independent of traditional risk factors. A diagnosis of hypertension is associated with augmented asthma severity, and reduced lung function has been correlated with heightened cardiovascular mortality.Given the bidirectional relationship between compromised lung function and compromised cardiovascular function, the rationale for treating and controlling hypertension in persons with asthma is compelling. Although the effect of blood-pressure control on asthma is largely unexplored , and the aim of this report is to discuss the potential mechanistic links between hypertension and asthma, the influence each condition has on the other, and approaches to the treatment of hypertension in adult patients with asthma.

Introduction :

Asthma is currently understood as a disorder that is characterized by two main endotypes: type 2 high inflammation and type 2 low inflammation. These subtypes are broadly defined by their predominant underlying mechanism, which is largely determined by the T cells or innate lymphocytes and cytokines that are involved. Each endotype can be further subdivided into multiple phenotypes that are distinguished by clinical features, pathological findings, and biomarkers (chemokines). Owing to the lack of uniform criteria for classifying types of asthma [1], estimates of the prevalence of type 2 high- and type 2 low-inflammation endotypes vary; however, each endotype appears to represent approximately half the population with asthma The degree of inflammation in patients with hypertension and asthma reflects the conjoint effect of both conditions[1]. Hypertension skews T cells toward a proinflammatory (type 1 helper T-cell [Th1 cell]) phenotype, characterized by increased interferon-γ responses and decreased type 2 helper T-cell (Th2 cell) responses[1]. In asthma, enhanced airway hyperresponsiveness and severe disease are associated with elevated levels of interferon-γ3Correspondingly[8], in hypertension, interferon-γ and Th1-cell polarization contribute to blood-pressure elevation and its sequelae.[2] , Interleukin-17 has also been shown to play a major role in the development of hypertension and its related end-organ damage in both studies in animals and in vitro models. Interleukin-17 induces a proinflammaory vascular smooth-muscle cells by enhancing the release of mediators, including interleukin-6[2]

Methods and Materials :

The Severe Asthma Research Program conducted multiple studies in which patients with asthma were grouped into discreet clusters on the basis of a hierarchical analysis of variables that included clinical characteristics[3], biomarkers, cellular profiles, lung function, atopic status, responses to treatment, gene expression, and coexisting conditions[4] It is notable that two studies that included hypertension as a variable showed cosegregation of hypertension with asthmatic profiles that are typical for the type 2 low-inflammation endotype.[3] Patients with features of the type 2 low-inflammation endotype (older age, later onset of asthma, higher body-mass index [BMI], greater severity of disease, and low atopy) were also more likely to have hypertension (48 of 175 patients [27%]) than patients with the type 2 high-inflammation endotype (50 of 551 patients [9%]).[5]

Results :

The results of a separate study based on clinical characteristics and assessments of inflammatory cells in blood and sputum showed a significantly higher incidence of hypertension in clusters distinguished by severity of disease, older age, later onset of disease, higher BMI, and greater resistance to treatment with glucocorticoids: 31% (51 of 164 patients) as compared with 11% (28 of 259 patients).[3] These observations suggest that type 2 low inflammatory pathways may provide a pathogenic mechanism that links these two diseases.

Discussion :

CXCL8 and CXCL10, and C-reactive protein. Both anti–interleukin-17 treatment and genetic deletion have been shown to reduce hypertension in studies in animals.[6],A role for interleukin-17 is also evident in some patients with severe asthma in whom an elevated level of interleukin-17 is correlated with neutrophil infiltration[7], airway hyperresponsiveness, and a lack of sensitivity to glucocorticoids. In these patients, interleukin-17 is capable of inducing secretion of proinflammatory cytokines from lung structural cells and airway smooth muscle[7], including tumor necrosis factor α, interleukin-1β, granulocyte colony-stimulating factor[7], and interleukin-6 as well as the chemokines CCL11 (eotaxin) and CXCL8 (interleukin-8), which are important in airway inflammation and remodeling[7]. Surprisingly, in one trial, the targeting of interleukin-17 failed to ameliorate symptoms in patients with severe asthma[7]; however, a subgroup analysis identified patients with highly reversible depression in FEV1 who had some improvement, as reflected by the Asthma Control Questionnaire. The functional role of interleukin-17 in the contraction of smooth-muscle cells may offer a partial explanation for the more favorable response in this subgroup[8] , Experimental evidence supports the concept that elevated interleukin-6 levels can drive the differentiation of CD4+ T cells through interaction with transforming growth factor β to promote skewing toward type 17 helper cells (Th17) cells, leading

to a reduction of regulatory T cells (Tregs). Tregs play a protective role in the development of hypertension that is related in part to production of interleukin-10[6] and play a critical role in the regulation of asthma development.[9]

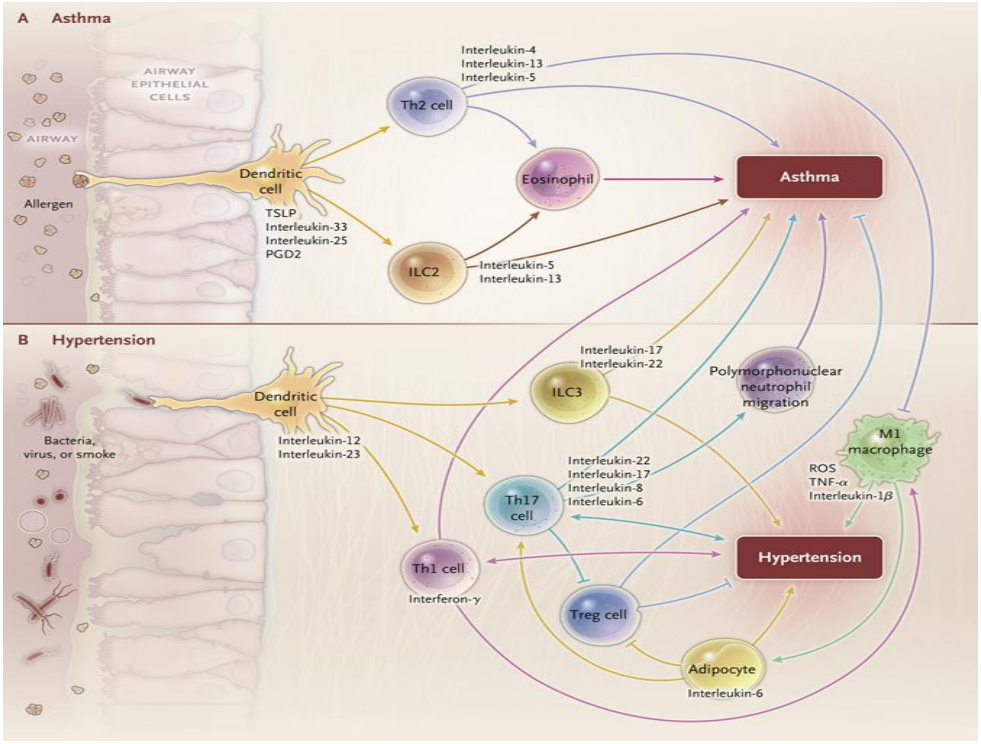

Figure1. inflammatory pathways in patients with Asthma who have hypertension.

Treatment :

What does the treatment of hypertension generally accomplish, and how might that treatment affect patients with asthma? To date, all-cause mortality has not differed significantly among patients with hypertension treated with any of the four major classes of first-line antihypertensive agents[10].The degree of blood-pressure reduction rather than the choice of antihypertensive medication appears to be the major determinant of outcome In patients with asthma, however, additional issues related to various pharmacologic agents should be considered[10]
Beta Blockers ; Some caution should be used when introducing beta-blockers to patients with asthma owing to concerns regarding both unopposed bronchoconstrictive signals and therapeutic response to β2-agonists[11]. Furthermore, beta-blockers are not generally recommended as monotherapy for the treatment of hypertension in patients with most conditions, although there may be specific indications for patients with congestive heart failure who have arrhythmias or who have had myocardial infarction[12], Angiotensin-Converting–Enzyme Inhibitors; As is the case in the general population of patients with hypertension, angiotensin-converting–enzyme (ACE) inhibitors are useful in patients with asthma and hypertension — they are not contraindicated[13].

Conclusions :

Persons with both hypertension and asthma represent an important subset of the globally escalating number of persons with cardiovascular and airway disease. Experimental evidence from studies in animals and observations in human disease highlight smooth-muscle activation, vascular dysfunction, and systemic inflammation as unifying characteristics within this cohort. The influence of type 1 and type 17 inflammatory pathways is noteworthy for increasing the severity of disease in patients who have hypertension and severe asthma who are also obese and have metabolic dysfunction. The treatment of patients with both hypertension and asthma should involve an integrated approach that includes pharmacotherapy and changes in lifestyle. A combination of interventions — including diet modification, salt restriction, stress reduction, and weight loss — that target shared pathophysiological mechanisms may be of value for these patients.

Future work :

The role of Hypertension in patients with asthma is largely unexplored. Considering the mechanistic relationship between asthma and Hypertension many factors are involved. These factors are mainly attributed either to environmental changes or/and to changes relating to both diet and life style. There is an interaction between innate and adaptive immune response, alterations in microbiome and enhanced T1 and T17 inflammatory processes. These alterations lead to remodeling of smooth muscle cells and affect in different directions either the blood vessels or/and the airway. The above mechanistic view may also have implications in the disease management and particularly in treatment strategies. The first approach is to control both diseases with the respective treatment strategies, to modify lifestyle factors and to treat co-existing diseases like sleep apnoea. Interestingly some of the pharmacologic agents used for both diseases may have some specific considerations due to possible side effects

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