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YURAK ISHEMIK KASALLIGI MAVJUD BEMORLARDA INTERLEYKIN-6 AHAMIYATI

G`opirjonova D.D., Alyavi A.L.
Toshkent tibbiyot akademiyasi

Annotatsiya. Yallig`lanish bu yurak ishemik kasalligida (YuIK) ishtirok etuvchi muhim jarayon hisoblanadi. Metabolik stress, gemodinamik ortiqcha yuk va endoteliy va miyokard hujayralarida neyrogumaral giperaktivatsiyaga javoban interleykin (IL) 1 va 6 kabi yallig`lanishga qarshi sitokinlar chiqariladi. Dastlab, bu jarayon organizimni stresga moslashishini taminlaydi, ammo keyinchlik kasallik davrida ular endothelial va yurak disfunktsiyasi orqali miyokard fibroziga olib keladigan zararli ta`sirlarni keltirib chiqaradi. Tadqiqotlar shuni ko`rsatadiki yurak ishemik kasalligida bemorlarda interleykin(IL)6 yallig`lanish mediatori ko`payib ketadi.

Kalit so‘zlar: Yurak ishemik kasalligi, biomarkerlar, yallig`lanish, interleykin-6

ЗНАЧЕНИЕ ИНТЕРЛЕЙКИНА 6 У БОЛЬНЫХ С ИШЕМИЧЕСКОЙ БОЛЕЗНЬЮ СЕРДЦА

Гопиржонова Д.Д., Аляви А.Л.
Ташкентская медицинская академия

Аннотация. Воспаление вовлечено в патогенез ишемической болезни сердца (ИБС). В ответ на метаболический стресс, гемодинамическую перегрузку и нейрогормональную гиперактивацию в эндотелии и клетках миокарда высвобождаются провоспалительные цитокины, такие как интерлейкин (IL) 1 и 6. Первоначально эти маркеры способствуют адаптации сердечно-сосудистой системы к стрессу, но на более позднем этапе заболевания они оказывают вредное воздействие через эндотелиальную и сердечную дисфункцию, приводящую к фиброзу миокарда [1]. Предыдущие исследования показали увеличение маркера воспаления, такого как интерлейкин (IL) 6, у пациентов с ишемической болезнью сердца.

Ключевые слова: ишемическая болезнь сердца; биомаркеры; воспаление; интерлейкин-6.

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FEATURES OF INTERLEYKIN-6 IN PATIENTS WITH ISCHEMIC HEART DESEASE

G`opirjonova DD., Alyavi A.L.
Tashkent Medical Academy

Annotation. Inflammation has been implicated in the pathogenesis of ischemic heart disease (IHD). In response to metabolic stress, hemodynamic overload, and neurohormonal hyperactivation in the endothelium and myocardial cells, proinflammatory cytokines such as interleukin (IL) 1 and 6 are released. Initially, these markers favor the adaptation of the cardiovascular system to stress, but later in the course of the disease, they produce deleterious effects through endothelial and cardiac dysfunction leading to myocardial fibrosis [1]. Previous studies have shown an increase in inflammatory marker such as interleukin (IL) 6 in patients with ishemic heart disease

Keywords: ischemic heart disease; biomarkers; inflammations; interleukin-6.

Ischemic heart disease (IHD) is the major cause of death all over the world according to the report of World Health Organization. The use of Interleykin-6 has aroused interest in cardiovascular medicine because of the direct action of these factors on several cell functions such as adhesion, proliferation, migration, and others. Functional pleiotropy and redundancy are characteristic features of cytokines. Interleukin 6 (IL-6) is a typical example: IL-6 induces cellular differentiation or expression of tissue-specific genes; it is involved in processes such as antibody production in B cells, acute-phase protein synthesis in hepatocytes, megakaryocyte maturation, cytotoxic T cell differentiation, and neural differentiation of PC12 (pheochromocytoma) cells. It promotes growth of myeloma/plasmacytoma cells, T cells, keratinocytes and renal mesangial cells, and it inhibits growth of myeloid leukaemic cell lines and certain carcinoma cell lines. The IL-6 receptor consists of two polypeptide chains, a ligand-binding chain (IL-6R) and a non-ligand-binding, signal-transducing chain (gp130). Interaction of IL-6 with IL-6R triggers the association of gp130 and IL-6R, and the signal can be transduced through gp130. Association of gp130 with IL-6R is involved in the formation of high affinity binding sites. This two-chain model has been shown to be applicable to receptor systems for several other cytokines, such as granulocyte-macrophage colony-stimulating factor (GM-CSF), IL-3, IL-5 and nerve growth factor (NGF). The pleiotropy and redundancy of cytokines may be explained on the basis of this unique receptor system.

IL-6 expression is mostly modulated by the nuclear factor kappa B (NF-KB). NFKB proteins are maintained in the cytoplasm by their binding with inhibitory proteins (IKBs).

Cytokines, infections, and toxins can induce the phosphorylation, ubiquitinization, and subsequent degradation of the IKB protein by the proteasome. This allows NF-KB to translocate to the nucleus and bind cognate DNA-binding sites to regulate the transcription of a large number of genes, including inflammatory cytokines . However, the potential utility of inflammatory markers in the diagnosis, treatment, and prognosis of this syndrome has not yet been clarified. The need to clarify the potential utility of these markers in the diagnosis, risk stratification, or even therapeutic targets in heart failure has been investigated in current clinical trials. In this respect, the studies ATTACH and RENEWAL targeting TNFα did not have relevant clinical results in HF. In contrast, the CANTOS study recently demonstrated that canakinumab, a monoclonal antibody that binds and blocks interleukin IL-1, reduces the risk of major adverse cardiovascular events (MACE) without affecting lipid levels in patients with a history of acute myocardial infarction with elevated CRP. The cardiovascular benefits increased as CRP was reduced. A secondary analysis of the CANTOS study found that IL-6, a pro-inflammatory cytokine normally stimulated by IL-1β, could play a fundamental role in both global and cardiovascular prognosis.

Characteristics of the study population and comparison between both groups

	Total(N=78)	IL6Normal(N=36)	IL6High(N=42)	P
Age in years—median (SD)	73.2 ± 5.4	71.5 ± 3.3	76.8 ± 6.8	0.354 a
Sex female-n(%)	45(19)	22(51.3)	24(56.5)	0.890b
Smoking	4(4.1)	3(4.1)	2(4.6)	0.820b
Sedentary	45(60.4)	20(48.4)	26(62.1)	0.490b
Underlying cardiomyopathy	31(43.2)	18(45.1)	16(34.6)	0.301b
Ischemic cardiomyopathy	16(23.0)	4(14.4)	11(36,2)	0.213b

Conclusions. IL-6 was elevated in a subgroup of patients with ischemic heart desease, dyslipidemia, atrial fibrillation diabetes mellitus, anemia, and chronic renal failure as already described. In this respect, anemia, chronic renal failure, and atrial fibrillation were the conditions independently associated with elevated IL-6 levels. Therefore, in our study, mortality was higher, and we observed a tendency of higher hospitalization in ischemic heart desease with elevated IL-6.

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