THE AGGRESIVITY FACTORS AND THE ATHEROSCLEROTIC PLAQUE

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Abstract

Atherosclerosis is a multifactorial disorder, among the traditional risk factors are: age, masculine sex, dyslipidaemia, arterial hypertension, diabetes mellitus, smoking, sedentary, and abdominal obesity – clinical marker of hyperinsulinism, metabolic syndrome, unhealthy life style, heavy alcohol consumption, depression. The metabolic syndrome has been associated with a procoagulant state increasing circulation concentrations of fibrinogen and plasminogen activator inhibitor-1, and increasing atherogenic small, dense LDL particles. Insulin resistance itself predisposes to CHD, or gives rise to the other components, many of the clustered factors are associated with risk for atherosclerosis or thrombosis. Atherogenic dyslipidaemia is the combination of low quantities of HDL-col, elevated small dense LDL and plasma TG. Risk factors tend to cluster and interact together and induce the coronary heart disease (CHD), morbidity and mortality. Low saturated fat and cholesterol diet is the key lifestyle change required for decreasing LDL- col, and in addition a high-carbohydrate diet may dramatically increase triglyceride (TG). Vascular endothelium has a central place in pathogeny of atherosclerosis. Nitric oxide is the most potent endogenous vasodilatator. Changing the risk factors constitutes the major therapeutic objective in patients with or without clinical manifestations of atherosclerotic disorder.

Key words*: thrombogenesis, vascular endothelium, macrophage, CHD*

Introduction

The world coronary disease mortality is alarming, in 2000 being registered 8 millions demises, and the estimations for 2020 are very dark, about 11 billiards demises.

Atherosclerosis is a multifactor disorder, among the traditional factors are: age, masculine sex, dyslipidemy, arterial hypertension, diabetes mellitus, smoking, sedentary, and abdominal obesity – clinical marker of hyperinsulinism, unhealthy lifestyle, such as stress.

*Transformations of vascular endothelium in atherosclerosis: v*ascular endothelium occupies a central place in atherosclerosis pathogeny, being compromised by activation of endothelial cells, it increases trans endothelial permeability of atherogenic lipoproteins LDL- col, by active way- endocitosis, or by passive way- transcitosis, LDL being oxidated in macrophages. At the vascular endothelium level it decreases vasodilatation that compromises hemodynamic control, it liberates endoteline with a strong vasoconstrictor effect [1].

The formation of atheromatosis plaque begins with lipidic layers through subendothelial diapedesis of monocites, transformed in macrophages; then it takes place the activation of smooth muscular cells with the progression of primary lesions of lipidic layers, being formed fibrosis head of atherosclerotic plaque, made of collagen, proteoglicans and smooth muscular fibres, intimaly prolipherative and covered by endothelial cells; then it takes place the continuous accumulation of lipids in lipidic endothelium that brings cellular death.

There are more endogen factors that are responsible in vulnerability of unstable atherosclerotic plaque [2,3].

- macrophages have an essential role in plaque vulnerability because they stimulates the release of cytokines that lead to vascular wall inflammation, it stimulates the release of tisular factor which initiates coagulation and thrombogenesis;
- the increase of coagulation facilitates thrombosis and increases predisposition to instability and break of plaque.
- the tisular factor initiates coagulation and ends with thrombus formation.

Oxidated LDL stimulates the activity of tisular factor and stimulates the production of plasminogen activator that inhibits fibrinolisis and at the end, the hypercoagulation surrounding the plaque, and formation of the thrombus surrounding the unstable break plaque [4, 5].

The damage of unstable plaque takes place by cracks, fissure, breaking and then begins thrombogenesis that has two major results: partial occlusion-parietal thrombus-rich in fibrine and thrombocites with clinically manifestation of unstable angine leading in the same time distal occlusion and emboli, or total occlusion-thrombus rich in thrombin [6, 7].

How do we interfere in order to reduce the formation of atherosclerotic plaque?

Changing the risk factors constitutes the major therapeutic objective in patients with or without clinical manifestations of atherosclerotic disorder.

- chronic hyperglycemia helps the accumulation of proteins in blood, that induce the increasing of vascular permeability, with repercussions on stimulating oxidation of LDL-LP and in the same time has a direct mechanism of citotoxicity, increasing the production of cytokines, maintaining the inflammation of vascular wall and having vasospastic effect.
- dyslipidemia - strong atherogenic lipoproteins (LDL, rich in Lp-B, C-III), penetrates the arterial wall and induce moleculary adhesion, separates macrophages and increase caption levels of LP. Lipid accumulation in the arterial wall, from LDL, considered the key atherogenic lipoprotein and perhaps from remnants of TG-rich lipoproteins-is requisite to the formation of fatty streaks, wich are the precursors of atherosclerotic plaques.
- arterial hypertension – atherosclerosis hemodynamic factor- it creates a stress intraarterial aria that reflects over

endothelial permeability, increases time contact of LP with the endothelium, helps Lp penetration, decrease endothelial vasodilatation.

How we reduce the risk of breaking plague?

- by stabilizing the plaque- the decrease of lipidic nucleus, decrease of inflammation of vascular wall, stabilizing the fibrosis head.
- by decreasing risk factors - decreasing mechanic stress, of arterial tension, of cardiac frequency, reducing inothropism.

The factors of plaquetary vulnerability are:

- reduced lipidic nucleus
- thick fibrosis head
- wide lipidic nucleus
- parietal inflammation
- thin fibrosis head
- unstable plaque

The major therapeutic target is the decrease of lipidic nucleus and the concentration of macrophages, that decrease the inflammation of vascular wall and it stabilize fibrosis head of the plaque.

Stabilization of atherosclerotic plaque is realized by: reducing blood pressure; decreasing cardiac frequency; reducing heart contractility; changing vulnerable factors.

How we reduce thrombosis risk?

- decreasing thrombocite's adhesion (a)
- inhibit of plaquetary aggregation (b)
- reducing thrombus formation (c)

The effect of statines at vascular wall level:

– the statines operates at the arterial vascular wall, having effect on endothelial cells, it decrease the production of cytokines and of tisular factors. The pleiotropic effects, include improvement of endothelial function, anti-inflammatory effects, antioxidant effect, and plaque stabilization. The statins lower plasma levels of CRP, a measure of inflammation. Pleiotropic effects occur soon after initiation of statin therapy.

PPARα activators have effect over more factors involved in atherosclerosis process, by two main mechanisms:

- metabolic and vascular action
- anti-inflamatory and anti-thrombotic effects.

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