Mechanisms of atherosclerosis development and some problems of its treatment

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Механизмы развития атеросклероза и некоторые вопросы его лечения

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Abstract: *development mechanisms of atherosclerotic process are analyzed in the work. There are considered schemes of action mechanism of remedies causing reduction of atherogenic substances in blood plasma both by way of their accelerated removal from blood plasma, and via blocking of their synthesis, as well as remedies oppressing the processes of free-radical oxidation.*
Creation of combination medications is offered, which conjoin abovementioned action mechanisms with different dominant impacts, depending on degree of manifestation of pathological state that will promote successful differentiated therapy.
Аннотация**:** *в работе проанализированы механизмы развития атеросклеротического процесса. Рассмотрены схемы механизмов действия средств, вызывающих снижение атерогенных субстанций в плазме крови как путем их ускоренного вывода из плазмы крови, так и путем блокирования их синтеза, и средств, угнетающих процессы свободно-радикального окисления.*
Предложено создание комбинированных препаратов, сочетающих вышеуказанные механизмы действия с разными преимущественными влияниями, в зависимости от степени выраженности патологического состояния, что будет способствовать успешной дифференцированной терапии.

Keywords*: atherosclerosis, atherogenic substances, statins, cholestyramine, prostacyclinotherapy.*
Ключевые слова*: атеросклероз, атерогенные субстанции, статины, холестирамин, простациклинотерапия.*

Development of atherosclerosis is promoted by many factors of different nature, respectively different mechanisms form the basis of its development and differentiated approach is necessary for its treatment [1, 3, 5, 7].

Development of atherosclerosis is accompanied with intimal thickening of blood vessel walls, formation of cholesterol plaques that is caused by high blood cholesterol and permeability of intima cells in relation with cholesterol, increase of peroxide oxidation of lipoproteins [2, 4, 8].

Accumulation of cholesterol in arterial intima is followed by organic vasoconstruction and possible thrombus formation, lipidosis and calcinosis, cerebral ischemia, development of myocardial infarction and insult.

Therapeutic approach to atherosclerosis, along with decrease of dietary cholesterol foresees reduction of atherogenic substances (lipoproteins with low and very low density and cholesterol) in blood plasma, on one hand, and increase of content of lipoproteins with high density, on the other.

Content of abovementioned lipoproteins can be decreased both by way of their accelerated removal from blood plasma, and via blocking of their synthesis.

Let's consider the mechanisms of hypolipidemic effect of statins. Statins cause hypolipidemic effect, while blocking the cholesterol synthesis in liver, promoting increase of lipoproteins' receptors, reduction of low and transmission density lipoproteins in plasma, decrease of dietary cholesterol (diagram № 1).

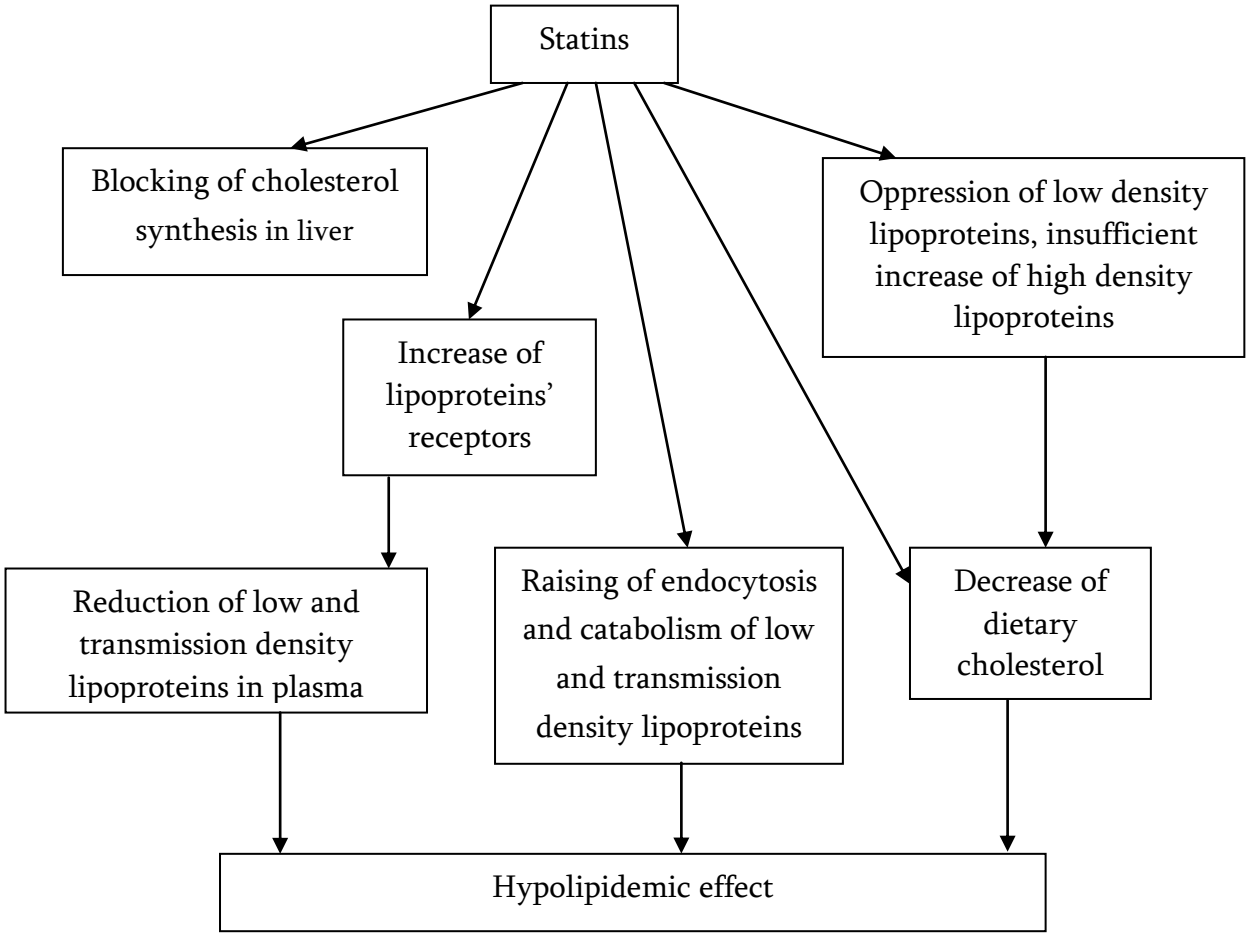
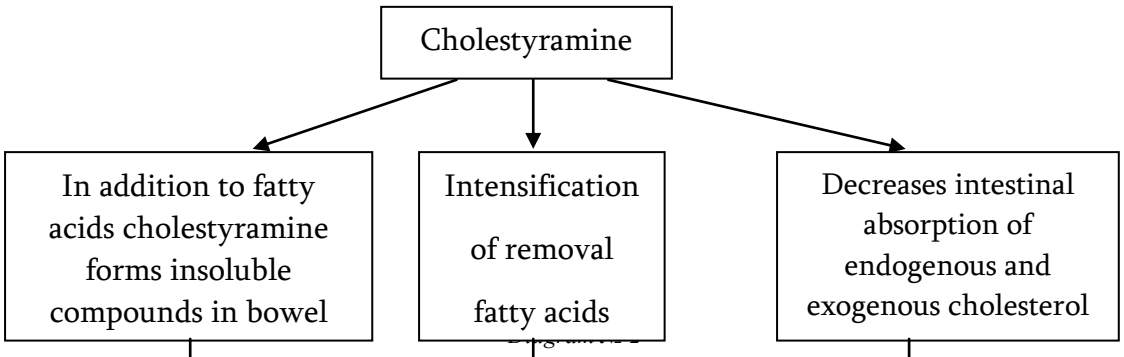


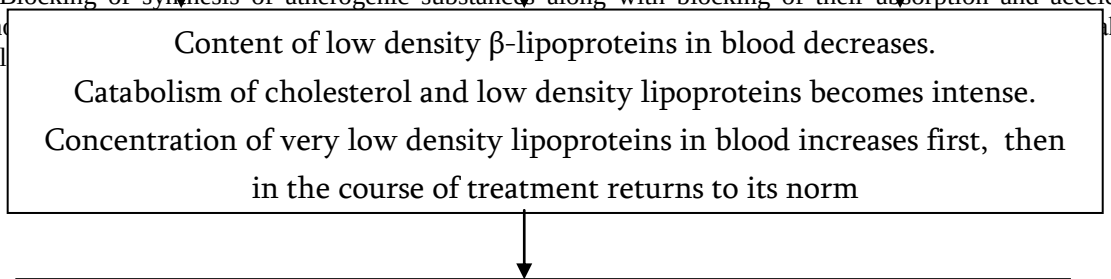
Diagram № 1. Action mechanism of statins blocking cholesterol synthesis

Accelerated removal of cholesterol and fatty acids from organism is promoted by preparations of cholestyramine group.

Let's consider action mechanism of cholestyramine intensifying the removal of cholesterol and fatty acids (diagram № 2).



Blocking of synthesis of atherogenic substances along with blocking of their absorption and accelerated remo ake of chol



As far as free-radical oxidation of proteins is accompanied with atherosclerotic process, administration of medications against free-radical oxidation is of special importance for blocking of atherosclerotic process [6, 9].

Active forms of oxygen, while having clearly manifested toxic action, have a direct effect on ferments, proteins and cell membrane, and besides they cause pathological stimulation and intensification of processes of lipid peroxidation.

Prostacyclinotherapy is of high importance at that time. Lipid peroxidation during hyperlipidemia promotes oppression of prostacyclin synthetase. That's why stimulators of prostacyclin synthesis or medications acting against lipid peroxidation have an effect on prostacyclin synthetase, assist accumulation (deposition) of endogenous prostacyclin, increase of c-AMP in thrombocytes and endothelium, reduction of thrombocytes aggregation and adhesion, endothelium conduction, lipoprotein molecules penetration into sub-endothelium and inhibit formation of atherosclerotic plaques (diagram № 3).

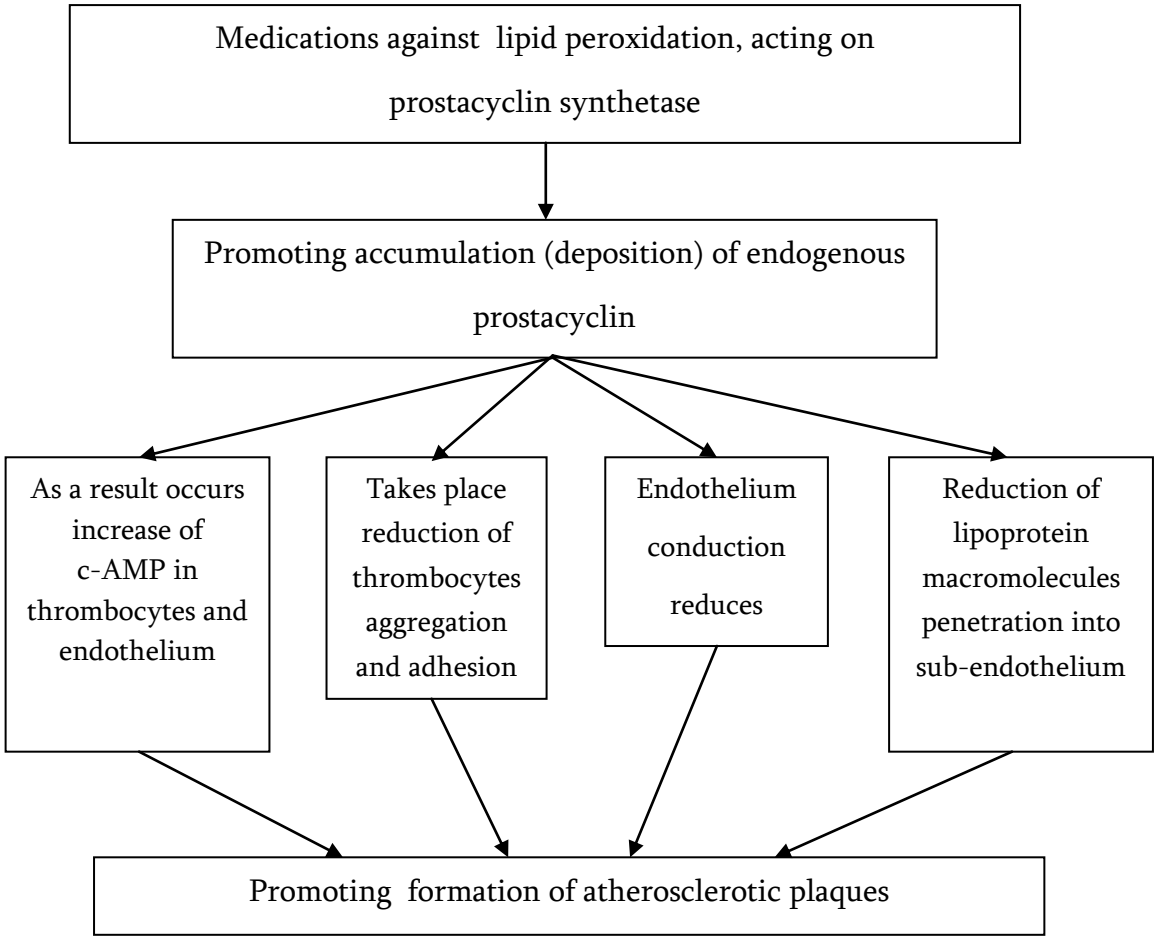


Diagram № 3

Thus, based on abovementioned, it would be expedient to create combination medication, which conjoin opportunities of blocking of synthesis of atherogenic substances, intensification of their removal from organism, blocking the processes of free-radical oxidation with different dominant impacts, depending on degree of manifestation of pathological state that will promote successful differentiated therapy.

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