Original Article

Gut Microbiota Metabolites As A New Therapeutic Target In Patients With Coronary Artery Disease And Atrial Fibrillation

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Abstract

The aim: To reveal new peculiarities of gut microbiota metabolites in CAD patients with or without AF and to detect special connections toward ones with clinical and laboratory features of investigated groups.

Materials and methods: 300 patients were investigated. They were divided into 3 groups: control group – 28 patients without CAD and arrhythmias; main group – 149 patients with CAD but without arrhythmias; comparable group – 123 patients with CAD and AF paroxysm. Plasma TMAO, TMA, fecal SCFA levels was determined by gas chromatography with mass electron detection.

Results: Metabolomic analysis of the gut microbiota metabolites (plasma TMA, TMAO, fecal SCFA) and clinic-laboratory factors in patients with CAD and AF paroxysm was done in our study. We checked gut microbiota metabolites changes that are common for patients with CAD and AF comparable with CAD patients: increasing of TMA, TMAO plasma levels, fecal valeric acid level (13,88%, 36,52% and 1128,43% respectively, $p<0,05$) and decreasing total amount of fecal SCFA, USFA, MCFA, butyric, isovaleric, caprylic acids levels (17,09%, 38,16%, 95,54%, 78,75%, 56,29% and 99,21% respectively, $p<0,05$). Reliable correlations between CAD and AF with TMA, TMAO plasma and fecal SCFA levels were revealed by them and age, BMI, GFR, total cholesterol, TG, LDL, HDL, ApoB levels ($|r|>0,3$, $p<0,05$) were revealed that are known risk factors of CAD and AF. Moreover, TMAO, TMA, butyrate, total SCFA, USFA, MCFA levels are closely connected with IL-6 and CRP levels ($|r|>0,3$, $p<0,05$).

Conclusions: Gut microbiota metabolites (TMA, TMAO, SCFA, MCFA, USFA, butyric acid) are the new promising therapeutic targets for pathogenetic treatment and prevention AF paroxysm in CAD patients.

Keywords: coronary artery disease (CAD), atrial fibrillation (AF), gut microbiota composition, trimethylamine-N-oxide (TMAO), trimethylamine (TMA), short chain fatty acids (SCFA)

Introduction

Coronary artery disease (CAD) is the most common cardiovascular disorder while atrial fibrillation (AF) is the most common cardiac arrhythmia. Number of patients with CAD and AF increasing every year: presence of CAD increased risk of AF development and vice versa.

This can be explained by the similarity in etiology and pathogenesis of CAD and AF. Both diseases share associated risk factors – arterial hypertension, diabetes mellitus, chronic kidney diseases, obesity, heart failure and inflammatory diseases.

Dyslipidemia and chronic inflammation play the main pathogenetic role in CAD and AF development, but their real connections are still uninvestigated [1, 2, 3].

Gut microbiota – the complex of gut microorganisms. Today its role in cardiovascular diseases development was estimated: its impact on metabolic disorders as obesity, diabetes mellitus, atherosclerosis has been already approved, but anti- and proarrhythmic properties are still unknown. Gut microbiota changes are pathogenetically connected with arterial hypertension, chronic kidney diseases, inflammatory diseases and heart failure, which are an important etiological factors of AF and CAD [4].

Gut microbiota can cause direct and indirect (through its metabolites) impact on lipid exchange and inflammatory processes. Its metabolites include trimethylamine (TMA)/ trimethylamine-N-oxide (TMAO)/ choline, short chain fatty acids (SCFA), lipopolisacharide (endotoxine)/ bacterial wall products, bile acids, phenilacetylglutamine and uremic toxins (p-cresol/ indoxyl) [4, 5]. Plasma amino acids composition can be also included in gut microbiota metabolites [6].

TMA is a product of gut microbiota which is produced from dietary choline, betaine or carnitine. TMAO is a product of TMA