SCREENING OF PRIMARY ALDOSTERONISM WITH A NOVEL RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM TRIPLE-A ANALYSIS

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Aim. Primary aldosteronism (PA) is a frequent cause of secondary hypertension and its screening is expected to become a routine evaluation in patients with hypertension. The interference of antihypertensive medications with the Aldosterone-to-Renin-Ratio (ARR) is a major confounder during screening testing. Renin-angiotensin-aldosterone-system (RAAS) triple-A analysis is a novel liquid chromatography/tandem mass spectrometry diagnostic assay that allows simultaneous quantification of aldosterone, equilibrium angiotensin I (eqAngI) and angiotensin II (eqAngII). The aim of the present study was to assess the reliability of RAAS triple-A analysis for PA screening.
Methods. We evaluated the diagnostic performance of the Aldosterone-to-AngII-Ratio (AA2R) and five renin based diagnostic ratios, differing in methods to determine aldosterone levels and renin activity, either based on chemiluminescence or radioimmunoassay.
Results. We enrolled a cohort of 110 patients with hypertension and suspected PA referred to a single hypertension unit (33 patients with confirmed PA and 77 with essential hypertension). All ratios showed comparable areas under the curves ranging between 0.924 and 0.970 without significant differences between each other. The evaluation of the AngII-to-AngI ratio revealed persistent ACE inhibitor intake in some patients as cause for suppressed renin-based diagnostic ratios, while AA2R remained unaffected, allowing a AA2-R-based PA screening in presence of ACE inhibitor. The optimal cut-off value for the AA2R was 6.6 [(pmol/L)/(pmol/L)] with a sensitivity and specificity of 90% and 93%, respectively, non-inferior to the ARR while pointing to the potential for an interference free application in patients under ACE-inhibitor therapy.
Conclusions. This study shows for the first time the accuracy and reliability of RAAS triple-A analysis for the screening of PA, even in the presence of therapy with ACE inhibitors. Combining information on drug efficacy and compliance monitoring with PA screening, this method might have a significant impact on the overall performance of PA screening.

IMPACT OF DIETARY CHOLINE ON ATHEROSCLEROSIS DEVELOPMENT IN CONVENTIONALLY RAISED APOE-KO MICE EXPRESSING DIFFERENT LEVELS OF APOA-I

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Aim. Gut microbiota can influence atherosclerosis development by metabolizing dietary choline: experimental and observational studies have highlighted a positive correlation between increased plasma choline-derived TMAO concentrations and adverse cardiovascular events. This study was aimed at investigating, for the first time, how apoA-I/HDL levels can influence atherosclerosis development by modulating gut microbiota composition.
Methods. Chow diets with different choline contents (0.09% or 1.2%) were administered for 20 weeks to conventionally-raised, atherosclerosis-prone mice expressing different levels of apoA-I: extremely low-HDL mice (A-IKO/EKO) or high-HDL mice, deficient for both murine apoA-I and apoE, but overexpressing human apoA-I (hA-I/A-IKO/EKO).
Results. Choline supplementation did not influence plasma cholesterol and triglyceride concentrations that were dramatically reduced in A-IKO/EKO vs hA-I/A-IKO/EKO mice. Atherosclerosis, evaluated at the aortic sinus and in the entire aorta, was unsurprisingly increased in A-IKO/EKO vs hA-I/A-IKO/EKO mice. Less predictably, choline supplementation significantly worsened plaque development only in hA-I/A-IKO/EKO mice (aortic sinus: 66,870±46,870 vs 147,360±42,750 mm2 in females; 63,691±37,432 vs 110,030±42,937 mm2 in males; aortic arch: 0.34±0.65 vs 3.29±3.65 % in females; 0.87±1.03 vs 2.45±2.59 % in males). To characterize plaque composition, O.R.O. staining for neutral lipids and Mac-2 specific IHC for macrophages were performed. An increased dietary choline content did not result in an increased deposition of neutral lipids nor of the amount of infiltrating macrophage in atherosclerotic plaques of both genotypes.
Conclusions. Our results indicate that dietary choline supplementation worsens atherosclerosis development only when apoA-I is expressed. Further studies are ongoing to better clarify:
1) how apoA-I can modulate gut microbiota composition (i.e. the presence of choline-degrading bacteria);
2) the pathophysiological mechanisms influenced by the choline-TMA-TMAO metabolic pathway.