Poster

[P27-5] P27-5: Cardiovascular drugs (2)

Chair: David A. Joyce, Australia

Wed. Sep 27, 2017 12:30 PM - 1:30 PM Annex Hall (1F)

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[P27-5-1] Effect of angiotensin II receptor blockers on serum levels of epoxyeicosatrienoic acids

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Keywords: epoxyeicosatrienoic acids, angiotensin II receptor blockers, multivariate analysis, arachidonic acid

Background

We previously demonstrated that several angiotensin II receptor blockers (ARBs) inhibit cytochrome P450 (CYP) involved in metabolism of arachidonic acid (AA) to reduce the production of epoxyeicosatrienoic acids (EETs) *in vitro*. EETs generated from AA by CYP enzymes exert biological functions such as vasodilation and anti-inflammation. EETs are further metabolized to less active dihydroxyepoxyeicosatrienoic acids (DHETs). The aim of this study was to evaluate the effect of ARBs on the serum levels of eicosanoids, the sum of EETs and DHETs, in patients by using multivariate analysis.

Methods

Ninety patients taking ARBs and 98 ARBs-free controls, admitted to Teine Keijinkai Hospital from October 2013 to October 2016 were included in the study. The study protocol was approved by the ethics committee of Teine Keijinkai Hospital. The serum concentrations of eicosanoids were determined by LC-MS/MS. Multivariate analysis adjusting for age, sex, body mass index, smoking, estimated glomerular filtration rate (eGFR), history of myocardial infarction, and medications (ARBs, HMG-CoA reductase inhibitors, anti-platelet drugs, anti-coagulant drugs, anti-diabetic drugs, calcium blockers, beta-blockers, and diuretic drugs) was performed using SPSS software.

Results

There were no significant differences in the serum levels of eicosanoids between the ARBs and control groups (p=0.110); however, the median value was 26% lower in the ARBs group (1.4 nmol/L) compared to the control group (1.9 nmol/L). Multivariate analysis showed that eGFR was negatively associated with the serum levels of eicosanoids (p=0.012), and ARBs significantly decreased the levels (p=0.021).

Conclusions

Multivariate analysis indicated the possibility that ARBs reduce the production of eicosanoids from AA *in vivo* . This result is consistent with our previous *in vitro* studies showing that several ARBs inhibit CYP enzymes. Increased serum levels of eicosanoids in patients with low eGFR could be attributed to delayed excretion of DHETs. Decreasing the serum levels of eicosanoids may attenuate its various biological effects. Further studies are necessary to compare the lowering effect of individual ARBs on serum eicosanoids levels and the relationship between serum eicosanoids levels and the risk of cardiovascular events.