Abstract: P3497

The functional roles of thromboxane A synthase 1 (TBXAS1) and miR-34b-3p in the pathogenesis of aspirin response

Authors:
WW Liu¹, ML Liu¹, ¹Peking University First Hospital, Department of geriatrics - Beijing - China,

Topic(s):
Platelets, Haemostasis, Coagulation

Citation:

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Background: Aspirin is widely used for prevention of cardiovascular diseases, but its antiplatelet efficiency varies individually. Insufficient inhibition of platelet aggregation during aspirin therapy is described as aspirin hyporesponsiveness and is recognized as a crucial risk factor for ischemic events. Aspirin hyporesponsiveness would be affected by multiple factors, while the mechanisms remain ambiguous.

Purpose: The present study aimed to evaluate aspirin response related gene profiles and potential regulating pathway using human blood samples and cell lines.

Methods: Patients with coronary artery disease who were under 100 mg/day aspirin treatment were enrolled. Written informed consent was obtained from every participant. Platelet function was measured by light transmission aggregometry (LTA) of arachidonic acid (AA) induced platelet aggregation. Expression of eight candidate genes and ingredients involved in AA metabolism was analyzed. Furthermore, potential mechanisms of varied aspirin response were investigated using megakaryocytic Dami cell lines.

Results: Human circulating mRNA levels of the eight candidate genes were evaluated, thromboxane A synthase 1 (TBXAS1) was the only one that showed significantly increased expression in the upper quartile of platelet aggregation (LTA-AA_Q4) group compared with the lower quartile of platelet aggregation (LTA-AA_Q1) group. Similarly, the expression of thromboxane synthase (TXS, the protein of TBXAS1) and thromboxane B2 (TXB2) was higher in the LTA-AA_Q4 group compared with the LTA-AA_Q1 group. The sequence complementarities of miRNA and targeted mRNA databases suggested a potential interaction between miR-34b-3p and TBXAS1. Further experiments proved that miR-34b-3p inhibits the translation of TXS by binding the untranslated region (3’-UTR) of TBXAS1 mRNA, resulting in a reduced TXB2 level. Although overexpressed miR-34b-3p had no distinct effect on cell proliferation, inhibited miR-34b-3p promoted megakaryocyte viability, which suggested that miR-34b-3p has a potential suppression on megakaryocyte proliferation.

Conclusions: Our data demonstrated that miR-34b-3p may facilitate the antiplatelet efficiency of aspirin by inhibiting TXS expression in elderly patients with cardiovascular diseases. To the best of the authors’ knowledge, this is the first study of its kind to investigate the regulatory mechanism of miR-34b-3p in AA metabolism and its potential association with aspirin responsiveness. This study provides a mechanism understanding of aspirin response related gene profiles and proposes a potential personalized aspirin use in terms of the expression of TBXAS1 and miR-34b-3p.
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