Effects of advanced glycation endproducts on uridine diphosphate-induced contraction in rat carotid artery

Mihoka Kojima, Takayuki Matsumoto, Keisuke Takayanagi, Kumiko Taguchi, Tsuneo Kobayashi

Dept. Physiol. and Morphol., Inst. Med. Chem., Hoshi Univ.

Advanced glycation end-products (AGEs) play a pivotal role in vascular function in various (patho)physiological conditions. Although uridine diphosphate (UDP) is an important extracellular nucleotide, the direct relationship between AGEs and UDP regarding their effects on vascular functions remain unclear. Therefore, we investigated the effects of AGE-bovine serum albumin (AGE-BSA) on UDP-mediated responses in rat carotid arterial rings. Concentration–dependent contraction but not relaxation was obtained following UDP application to carotid arteries with and without endothelia; the contraction was greater in the AGE-BSA-treated (0.1 mg/mL for 60 min) group than the control (1.0 v/v% PBS) group. The difference in UDP-induced contraction between the control and AGE-BSA-treated groups was not abolished by L-NNA [a nitric oxide synthase (NOS) inhibitor], whereas the difference was abolished by indomethacin [a cyclooxygenase (COX) inhibitor], ozagrel [a thromboxane synthase (TXS) inhibitor], and by SQ29548 [a thromboxane-prostanoid (TP) receptor antagonist]. The release of TXB_2, a metabolite of TXA_2, was increased by UDP in both groups, whereas the levels were similar between two groups. The release of PGE_2, other vasoconstrictor prostanoid, was similar among the groups (UDP-stimulated or -unstimulated control/AGE-BSA-treated groups). The contraction induced by U46619, a TP receptor agonist, in the presence of L-NNA was increased in the AGE-BSA-treated group compared with the control group. We conclude that the increase in UDP-induced contraction in the presence of AGE-BSA can be attributed to an increase in the COX/TXS/TP receptor pathway, in particular, TP receptor signaling.