Vasorelaxant effects of cromakalim on the rat aorta via Na-Ca exchange

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[Background]

Cromakalim exerts vasorelaxation, but its vasodilatory mechanism has not been fully elucidated yet. The objective of the present study was designed to elucidate whether cromakalim dilates the rat aorta by increasing the extrusion of intracellular Ca^{2+} via Na-Ca exchange or not. The degree of the contribution of Na-Ca exchange to vasodilatation is still controversial in the rat aorta.

[Methods]

The rat aorta, excised under anesthesia, was cut into helical strips and its endothelium was removed. The contractile force of the strips was measured in the Krebs-Henseleit solution.

[Results]

A K^+ channel opener, cromakalim ($10^{-7} \sim 3 \times 10^{-5}$ M) relaxed the A23187 (10^{-5} M)-induced contraction in the presence of nicardipine (3×10^{-6} M) in the rat aorta. However, the relaxant effect of cromakalim ($10^{-7} \sim 3 \times 10^{-5}$ M) on the A23187 (10^{-5} M)-induced contraction was attenuated in the presence of glibenclamide (10^{-5} M). Cromakalim ($10^{-7} \sim 3 \times 10^{-5}$ M) also relaxed the Na^+ -free-induced contraction in the absence of nicardipine, but the relaxant effect of cromakalim on the Na^+ -free-induced contraction was also attenuated in the presence of glibenclamide (10^{-5} M). The treatment with benamil (3×10^{-5} M) or KB-R7943 (10^{-5} M) suppressed the vasorelaxant effects of cromakalim ($10^{-7} \sim 3 \times 10^{-5}$ M) on the A23187 (10^{-5} M)-induced contraction in the presence of nicardipine (3×10^{-6} M). Caffeine (25 mM)-induced contraction was estimated in the presence or absence of cromakalim (10^{-5} M) in the Ca^{2+} and/or Na^+ -free solution. Cromakalim suppressed the caffeine-induced contraction in Ca^{2+} -free Krebs-Henseleit solution but not suppressed the caffeine-induced contraction in Ca^{2+} and Na^+ -free solution. The vasorelaxant effect of cromakalim was attenuated under the conditions without Na^+ - Ca^{2+} exchange function.

[Conclusions]

These results suggest that cromakalim exerted the vasorelaxant effects by promoting the forward mode Na^+ - Ca^{2+} exchange due to the membrane hyperpolarization to some extent, and this mechanism may especially be pivotal to reduce the increase in the cytosolic Ca^{2+} concentration in the rat aorta.