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Pharmacological evaluation of bradykinin effect on human umbilical artery in normal, hypertensive and diabetic pregnancy

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Abstract:
The objective of this investigation was to compare bradykinin (BK) action on isolated intact or denuded human umbilical artery (HUA) in normal pregnancy, pregnancy-induced hypertension (PIH) and gestational diabetes mellitus (GDM). Bradykinin contracted HUA in a concentration-dependent manner in all investigated groups. Control BK contractions were unchanged by L-NOARG (NO-synthase inhibitor), glibenclamide (K_{ATP} channel blocker), or des-Arg^9(leu^8)-BK (B_1 antagonist), while were reduced by indomethacin (cyclooxygenase inhibitior) or nifedipine (Ca^{2+} channel blocker). After endothelial denudation in GDM, concentration-response curve for BK was shifted to the left in relation to control HUA from normal pregnancy. OKY-046 (thromboxane A_2-synthase inhibitor) displaced concentration-response curve for BK to the right in PIH, whereas reduction in maximal contraction was obtained in HUA from GDM. Ouabain (Na^+/K^+-ATPase inhibitor) contracted HUA prior to BK addition in all groups. Apamin (small conductance K_{Ca} channel blocker), TEA (non-selectve K^+ channel blocker) or Ba^{++} ($K_{IR}{}^+$ channel blocker) augmented maximal BK contractions in normal pregnancy, PIH and GDM, respectively. HOE 140 (B_2 antagonist) produced concentration-dependent inhibition of BK effect in all groups. Collectively, in HUA from all groups BK evoked vasoconstriction *via* smooth muscle B_2 receptors. Intact endothelium provided additional modulation of BK contraction in GDM. Contribution of contractile cyclooxygenase products to BK action was demonstrated, and in PIH and GDM thromboxane A_2 was also involved. Voltage-gated Ca^{2+} channels and Na^+/K^+-ATPase contribute to the BK contraction, and to the regulation of basal vascular tone, respectively. Diverse K^+ channels modulate BK contraction in HUA by preventing excessive vasoconstriction.

Key words:
bradykinin, human umbilical artery, pregnancy-induced hypertension, gestational diabetes mellitus