MECHANISM UNDERLYING VASORELAXATION OF HUMAN SAPHENOUS VEIN INDUCED BY PROCYANIDIN B2

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Findings from epidemiological studies indicate that polyphenols, widespread in human diet and with numerous biological activities, act cardioprotectively. Procyanidins are subclass of polyphenols with high content in commonly consumed foods and beverages, such as grapes, tea, chocolate, nuts and apples. Cardioprotective abilities of procyanidins, might, at least partly, attribute to their vasodilator properties. Since exact mechanisms of procyanidin B2-induced vasorelaxation are unknown, our study aimed to investigate relaxant effect of procyanidin B2 on isolated human saphenous vein (HSV) and its underlying mechanisms. Discarded segments of HSV were collected from patients undergoing bypass surgery and studied in organ baths. Procyanidin B2 caused concentration-dependent relaxation of HSV precontracted by phenylephrine. The relaxation was strongly affected by inhibitors of NO/cGMP pathway, L-NAME, hydroxocobalamin and ODQ. Indomethacin, a cyclooxygenase inhibitor, significantly reduced only relaxation produced by the highest concentrations of procyanidin B2. Combination of apamin and TRAM-34, selective blockers of small- and intermediate-conductance Ca^{2+}-activated K^+ (K_{Ca}) channels (SK_{Ca} and IK_{Ca}), in the presence of L-NAME and indomethacin, did not additionally affect procyanidin B2-induced relaxation. Additionally, relaxation induced by procyanidin B2 was partially attenuated by 4-aminopyridine, predominant blocker of voltage-gated K^+ (K_V) channels, significantly inhibited by glibenclamide, selective ATP-sensitive K^+ (K_{ATP}) channels inhibitor, and almost abolished by iberiotoxin, highly selective blocker of large-conductance K_{Ca} (BK_{Ca}). Our results revealed that procyanidin B2 acts as a potent vasodilator on isolated human venous graft. Mechanism of this relaxation of HSV probably involves stimulation of NO production, as well K^+ channels opening, especially BK_{Ca}, and partially K_{ATP} and K_V.

MEHANIZAM VAZORELAKSACIJE HUMANE VENE SAFENE IZAZVANE PROCIJANIDINOM B2

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Nalazi epidemioloških studija ukazuju da polifenoli, široko rasprostranjeni u ljudskoj ishrani i sa brojnim biološkim aktivnostima, deluju kardioprotektivno. Procijanidini su podklasa polifenola sa visokim sadržajem u često konzumiranoj hrani i pićima, kao što su grožđe, čaj, čokolada, orašasti plodovi i jabuke. Kardioprotektivno delovanje procijanidina može se, bar delimično, pripisati njihovim vazodilatatornim svojstvima. S obzirom da tačni mehanizmi pomoću kojih procijanidin B2 izaziva vazorelaksaciju nisu poznati, cilj naše studije bio je da istražimo relaksantni efekat procijanidina B2 na izolovanoj humanoj veni safeni (HSV) i njegove osnovne mehanizme.Neiskorišćeni segmenti HSV su uzimani od pacijenata u toku bajpas operacija i ispitivani u kupatilu za izolovane organe. Procijanidin B2 izazvao je koncentracijski-zavisnu relaksaciju HSV prekontrahovane fenilefrinom. Na relaksaciju su snažno uticali inhibitori NO/cGMP puta, L-NAME, hidroksokobalamin i ODQ. Indometacin, inhibitor ciklooksigenaze, značajno je umanjio samo relaksaciju izazivanu najvećim koncentracijama procijanidina B2. Kombinacija apamina i TRAM-34, selektivnih blokatora Ca^{2+}-zavisnih K^+ (K_{Ca}) kanala male i srednje provodljivosti (SK_{Ca} i IK_{Ca}), u prisustvu L-NAME i indometacina, nije dodatno uticala na relaksaciju uzrokovanu procijanidinom B2. Osim toga, procijanidinom B2 izazvana relaksacija bila je delimično umanjena 4-aminopiridinom, dominantnim blokatorom voltažno-zavisnih K^+ (K_V) kanala, značajno inhibirana glibenklamidom, selektivnim inhibitorom ATP-zavisnih K^+ (K_{ATP}) kanala, i skoro potpuno blokirana iberiotoksinom, selektivnim blokatorom K_{Ca} velike provodljivosti (BK_{Ca}). Naši rezultati pokazuju da procijanidin B2 deluje kao moćni vazodilatator na izolovanom humanom venskom graftu. Mehanizam ove relaksacije HSV verovatno uključuje stimulaciju proizvodnje NO, kao i otvaranje K^+ kanala, posebno BK_{Ca}, i delimično K_{ATP} i K_V.