ジルチアゼムとベラパミルは低酸素化心臓からのアデニンヌクレオチド代謝物の消失を減少させる

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Diltiazem and Verapamil Reduce the Loss of Adenine Nucleotide Metabolites from Hypoxic Hearts

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ABSTRACT The present study was undertaken to elucidate possible mechanisms for a protection of myocardial cells from hypoxia-induced derangements in cardiac function and metabolism by calcium antagonists. For this purpose, rabbit hearts were perfused for 20 min under hypoxic conditions in the presence of 312 ng/ml diltiazem or 125 ng/ml verapamil, and then for 45 min under reoxygenated conditions. Metabolic changes in the myocardium and the perfusate were examined throughout. Hypoxia induced a marked decline in myocardial hygh-energy phosphates and an immediate release of ATP metabolites, such as adenosine, inosine and hypoxanthine, from the perfused heart. These changes were effectively depressed by diltiazem and verapamil. Hypoxia and subsequent reoxygenation resulted in a release of creatine phosphokinase from the heart, which was completely inhibited by the treatment with either diltiazem or verapamil. Myocardial calcum contents were increased by 20 min-hypoxic perfusion. Both diltiazem and verapamil protected the myocardium from calcium accumulation. The results suggest that diltiazem and verapamil are capable of preventing hypoxia-induced increase in the transmembrane feux of cellular components, which may be beneficial for the preservation of substabces necessary for the ATP regeneration after hypoxia and for the inhibition of calcium overload in cardiac cells.

抄録　本研究は低酸素負荷で発生する心機能，心筋代謝の悪化から心筋細胞を保護する作用

を示すカルシウム拮抗薬の作用機序について検討した。カルシウム拮抗薬としてはジルチアゼム，ベラパルミルを用いた。両薬物とも低酸素負荷で誘発される高エネルギーリン酸化合物の減少，ATP代謝物遊離の抑制を示した。また低酸素負荷後の再酸素化により発生するクレアチンキナーゼ遊離の抑制，カルシウム過負荷も両薬物で抑制された。以上の結果は両薬物が低酸素で誘発される心筋細胞内構成分の膜を介しての流出入を防御する可能性を示唆した。

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