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To clarify the vasoconstrictory action of LTD₄ on the injured coronary arteries, 8 mongrel dogs were denuded by balloon basket catheter (denuded group) and LTD₄ 0.33 μ g was directly administered into left anterior descending coronary artery. Hemodynamic parameters as well as epicardial ECG were recorded after LTD₄ administration. Another 8 non-denuded dogs were served as control. Furthermore, the influence of denudation to LTD₄-induced coronary spasm was determined by CAG and subsequently the pathological examination was made to evaluate the formation of coronary thrombus at the site of denudation. In results, a significant reduction in coronary blood flow and a significant increase in coronary vascular resistance concomitant with a marked prolongation of ST segment elevation on epicardial ECG were observed in denuded group as compared with non-denuded group. The exaggeration of LTD₄-induced coronary spasm at the site of denudation was documented by CAG and coronary thrombus formation was frequently in denuded group than non-denuded group (5/8 vs 1/8).

These results suggested that the vasoconstrictory action of LTD₄ was exaggerated on the injured coronary arteries and which might play an important role of pathogenesis and deterioration of myocardial ischemia.

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EFFECT OF LEUKOTRIENE ANTAGONIST (RS-411) ON LTD₄-INDUCED CORONARY SPASM

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We evaluated the action of Leukotriene D₄ (LTD₄) on coronary circulation and the effect of LT antagonist (RS-411) on LTD₄-induced coronary spasm in anesthetized dogs.

The dogs were administered LTD₄ 0.33 μ g into the left anterior descending artery (LAD) and hemodynamic parameters as well as epicardial ECG were recorded. Following the intracoronary administration of RS-411 50 μ g/kg (pretreatment), dogs were administered LTD₄ 0.33 μ g and recorded the same parameters. In 4 dogs, coronary angiography (CAG) was performed to study the effect of RS-411 on LTD₄-induced coronary spasm. In results, LTD₄ caused a significant reduction in coronary blood flow and a significant increase in coronary vascular resistance with a marked ST elevation on epicardial ECG. A significant increase in left ventricular end-diastolic pressure and a transient decrease in aortic pressure, mean coronary arterial pressure and aortic flow were observed with no effect in heart rate. No change in hemodynamic parameters were shown after the pretreatment of RS-411, and the duration of ST elevation was significantly shortened. CAGs documented the total occlusion of LAD in all dogs after intracoronary administration of LTD₄, but the degrees of coronary spasm were attenuated

by RS-411 in each dog.

These data suggest that RS-411 is effective to LTD₄-induced coronary spasm. It is also indicated that LTD₄ has direct coronary vasoconstrictory action and might play an important role in pathogenesis and deterioration of myocardial ischemia.

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EFFECTS OF LEUKOTRIENE C₄, D₄, AND FPL-55712 ON PROVOCATION AND PREVENTION OF CORONARY ARTERY SPASM IN MINIATURE PIGS

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Although an intracoronary administration (ic) of leukotriene (LT) C₄ and LTD₄ resulted in myocardial ischemia in animal experiments, the locus of vasoconstriction along the coronary vessel has not yet been elucidated. To determine whether LTC₄ and LTD₄ provoke coronary spasm (CS) at the large epicardial coronary artery, provocation of CS by LTs and prevention of CS by LTs blocker, FPL-55712, were examined angiographically in our swine model of CS. Eleven Göttingen miniature pigs underwent endothelial denudation (ED) of the left circumflex coronary artery and were fed a high cholesterol diet. Three months after ED, provocation of CS by histamine 10 μ g/kg ic after cimetidine 60 mg/kg iv was repeatedly confirmed angiographically at the site of ED and then, effects of LTs on coronary diameter and ECG-change were examined. LTC₄ and LTD₄ ic, in doses of 1 and 10 μ g, produced ECG-ST elevation when the contrast medium filled the large epicardial coronary artery more slowly ($p < 0.01$) than that of control angiograms. LTs constricted both the denuded and non-denuded sites of the large epicardial coronary artery equally less than 20%. FPL-55712 0.1 mg/kg iv prevented ECG-ST changes induced by LTs, but did not attenuate histamine-induced CS. Diphenhydramine, a H₁-blocker, 1 mg/kg iv abolished histamine-induced CS. Accordingly, in our swine model of CS, LTs constricted severely the small resistance vessels of the coronary artery but are not related to the mechanism of CS at the atherosclerotic portion of the coronary artery.

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EFFECTS OF THROMBOXANE A₂ ANALOGUE (STA₂), LEUKOTRIENE (LT) C₄ AND LTD₄ ON REGIONAL MYOCARDIAL BLOOD FLOW IN DOGS

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To study the role of Thromboxane A₂ (TXA₂), LTC₄ and LTD₄ in coronary circulation, we evaluated the effects of these substances and their antagonists on regional myocardial blood flow (MBF) in anesthetized dogs using heated cross-thermocouples method. STA₂, LTC₄ or LTD₄ was administered as a bolus into left anterior descending coronary artery (LAD). Aortic pressure was recorded and MBF was measured continuously in three areas; (1) LAD area = perfused area, (2) circumflex (CX) area = non-perfused area, (3)