Effects of lysophosphatidylcholine and palmitylcarnitine – lipid metabolites produced in ischemia – on porcine coronary and rabbit femoral arteries

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Summary: In organ bath experiments, amphiphilic lipids lysophosphatidylcholine (LPC) and palmitylcarnitine (PLC) produced a small increase in tension of nonprecontracted strips of porcine coronary artery with a subsequent decrease to initial level after high concentrations of the agents, both in intact and endothelium-denuded preparations. Both amphiphiles produced dose-dependent but incomplete relaxation of intact coronary strips precontracted with high potassium. The effect of PLC was more pronounced. LPC, $3 \cdot 10^{-4}$ mol·l$^{-1}$, did not influence Ca$^{2+}$-dose-response relationships, while PLC in concentration of $10^{-5}$ mol·l$^{-1}$ abolished the decline in the second Ca$^{2+}$-dose-response curve. Neither PLC nor LPC in concentrations of $3 \cdot 10^{-6}$ mol·l$^{-1}$ influenced endothelium-dependent relaxation produced by bradykinin precontracted with high potassium porcine coronary artery. Both amphiphiles did not change tension of nonprecontracted and precontracted with phenylephrine, $10^{-6}$ mol·l$^{-1}$, rabbit femoral artery ring segments or Ca$^{2+}$-dose-response relationships with and without endothelium.

Key words: amphiphilic lipids, lysophosphatidylcholine, palmitylcarnitine, coronary artery, femoral artery, endothelium-dependent relaxation

Introduction

A large body of evidence indicates that amphiphilic metabolites accumulated both within the myocardial cell and in the blood stream may play an important role in the pathogenesis of the cardiac abnormalities seen in patients with ischemic heart disease (1–5, 9, 10, 12). Amphiphilic lipids lysophosphatidylcholine and palmitylcarnitine produce electrophysiological changes of myocardial tissue similar to those seen during myocardial ischemia (5). Lysophosphatidylcholine increases coronary artery resistance in isolated rabbit hearts and contracts isolated canine coronary artery (1). In isolated rat heart perfused by Langendorf technique palmitylcarnitine produces initial vasoconstriction followed by prolonged vasodilation (7). In isolated precontracted with phenylephrine, rat thoracic aorta palmitoylcarnitine evokes dose-dependent but incomplete relaxation which decreases after endothelial removal, while having no influence on contractility of nonprecontracted tissue (7). In taenia preparation of guinea-pig caecum palmitoylcarnitine activates calcium channels (11).

The aim of the present investigation is to compare the effects of two amphiphilic lipids – lysophosphatidylcholine and palmitoylcarnitine – on resting and precontracted porcine coronary artery and rabbit femoral artery, and to study their influence on Ca$^{2+}$-dose-response relationships in the vessels.
Materials and Methods

Experiments were carried out on interventricular coronary artery from slaughterhouse pigs weighing 100-150 kg, and femoral artery of chinchilla rabbits 2.5-3.0 kg of weight. Isolated transverse strips (2.5 mm in width) of porcine coronary artery were set up in an organ bath filled with physiological salt solution (PSS) between two peripher clips, one of which was fixed to the bottom of the chamber and the other connected to isometric-force-displacement transducer WWH 141, VEB Messelektronik Dresden, GDR. The change in tension was registered on ink-writing recorder M1G1, VEB Carl Zeiss, Jena, GDR.

Ring segments (5 mm in width) of rabbit femoral artery were suspended in the organ bath between two nickel wire stirrups and the change in tension was registered by Gould UC-2 force displacement transducers on Dynograph R-711 (Beckman, USA). PSS composition (mmol·L⁻¹): NaCl 118, KCl 4.7, MgSO₄ 1.16, KH₂PO₄ 1.18, NaHCO₃ 15.0, CaCl₂ 2.52, Na-pyruvate 2.0, EDTA-Na-salt 0.026, glucose 11.0. PSS was saturated with carbogen, pH 7.35-7.40 and the temperature of the organ bath solution was thermostatically kept at 37°C. During the equilibration period (60-90 min) passive tension of coronary strips and femoral artery rings was adjusted stepwise to 40 mN and 20 mN, respectively. Organ bath solution was changed every 15 min during the equilibration period.

In part of the preparations, endothelium was removed by rubbing the intimal surface with a wooden applicator.

Two to three contractile reactions of coronary strips or femoral artery rings to potassium, 30 mmol·L⁻¹, or phenylephrine, 10⁻⁶ mol·L⁻¹, respectively, were performed to obtain stable contractile responses. Responses to bradykinin, 10⁻⁸ mol·L⁻¹, or acetylcholine, 10⁻⁶ mol·L⁻¹, respectively, were produced to check the presence or absence of endothelium before the experiments were started.

Lysophosphatidylcholine and palmitoylcarnitine were dissolved in drops of absolute ethanol, followed by dissolution in distilled water (10² mol·L⁻¹ stock solution). Phenylephrine stock solution (10⁻⁶ mol·L⁻¹) was made of distilled water. The desired concentrations of drugs were made in PSS; the concentrations shown in the text are final concentrations in the organ bath.

Effects on non-precontracted and precontracted vessel

After equilibration period or pretreatment of porcine coronary or rabbit femoral artery preparations with potassium, 30 mmol·L⁻¹, or phenylephrine, 10⁻⁶ mol·L⁻¹, respectively, amphiphilic lipids were cumulatively added into the organ bath when responses to the previous concentrations reached a plateau.

Effects on Ca²⁺-dose-response relationships

After equilibration period, artery preparations were incubated in Ca²⁺-free-hyper-K⁺-solution, 30 mmol·L⁻¹, plus 0.2 mmol·L⁻¹ of EDTA for 20 min, then washed with the same solution without EDTA and equilibrated for a further 30-40 min. Calcium from 1 mol·L⁻¹ stock solution was added directly to the organ bath to obtain increasing Ca²⁺-concentrations 0.1, 0.5, 1.0, 1.5, 2.0, and 2.5 mmol·L⁻¹. Concentrations of calcium were increased after tension reached a stable level (10-15 min intervals). After final Ca²⁺-concentration, wash-recovery cycle was repeated and the second Ca²⁺-dose-response curve was obtained. The agents studied were added into the organ bath 30 min before the second Ca²⁺-dose-response curve was started.

Effects on endothelium-dependent relaxation

After contractile responses of porcine coronary artery strips to potassium (30 mmol·L⁻¹) were stabilized, endothelium-dependent relaxation to increasing concentrations of bradykinin (10⁻⁶-10⁻⁷ mol·L⁻¹) was obtained. The preparations were washed with PSS and after 60 min of rest, precontracted by potassium, 30 mmol·L⁻¹, and a second dose-response curve to bradykinin was made. Vascular strips were washed again with fresh PSS. Amphiphiles were added to the organ bath 30 min before precontraction with potassium and bradykinin was introduced as above. The comparison of the bradykinin-evoked relaxation was made with the second dose-response curve since there was some weakening of relaxation response produced by higher concentration of bradykinin compared to the first dose-response curve.