Normalizan of HBOC-induced vasocclusion by simultaneous vasodilation in conscious, instrumented swine


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Abstract

NORMALIZATION OF HBOC-INDUCED VASOCCLUSION BY SIMULTANEOUS VASODILATOR ADMINISTRATION IN CONSCIOUS, INSTRUMENTED SWINE

Background: Most hemoglobin-based oxygen carriers (HBOCs) exert vasocclusion at increased heart rate, stroke volume, and afterload. This imposes a need to use HBOCs in conscious, instrumented swine, a model that mimics human conditions more closely than do anesthetized swine. Intravenous vasodilator therapy was needed to maintain normal coronary blood flow (CBF) during HBOC administration to swine. The aim of this study was to explore the potential for HBOC-induced coronary blood flow (CBF) vasocclusion to be reduced by simultaneous vasodilator therapy.

Methods: Swine were chronically instrumented for pulmonary artery pressure (PAP), aortic (MAP), and venous blood pressure (PV). HBOC-201 (GPD) was infused (2 ml/kg/min) in conscious, instrumented swine. Simultaneously, a vasodilator (NTG or ADO) was infused to normalize HBOC-induced increases in CBF. HBOC-201 had no effect on coronary blood flow at rest and during exercise.

Results: HBOC-201-induced increases in MAP were normalized by simultaneous NTG or adenosine (ADO) and NTG or ADO eliminated the effect. Exercise-induced increases in CBF were attributable primarily to increased heart rate; stroke volumes were essentially unchanged by ADO.

Discussion

The increase in mean arterial pressure during and following HBOC-201 infusion resulted in a modest decrease in cardiac output. This increase in cardiac output increased CBF at rest and during exercise. The increase in MAP and PAP, MW and myocardial metabolism occurred secondary to increased pulmonary vascular resistance (PVR). NTG, but not ADO, resolves HBOC-201-induced increase in pulmonary artery pressure (PAP). HBOC-201 had no effect on coronary blood flow (CBF) at rest and during exercise. HBOC-201 had no effect on mean arterial pressure (MAP) at rest and following HBOC-201 infusion.

Conclusions: HBOC-201-induced increases in MAP and PAP, MW and myocardial metabolism were abolished by HBOC-201, even during strenuous exercise. The HBOC-201-induced increases in MAP, MW and CBF can be prevented via simultaneous infusion of NTG or ADO.

Introduction

Most hemoglobin-based oxygen carriers (HBOCs) exert vasocclusion at increased heart rate, stroke volume, and afterload. This imposes a need to use HBOCs in conscious, instrumented swine. HBOC-201 (GPD) was infused (2 ml/kg/min) in conscious, instrumented swine. A vasodilator was infused to normalize HBOC-201-induced increases in CBF. HBOC-201 had no effect on coronary blood flow (CBF) at rest and during exercise.

Materials and Methods: Swine were chronically instrumented for MAP, PAP, PV, and CBF. HBOC-201 (GPD) was infused (2 ml/kg/min) in conscious, instrumented swine. Simultaneously, a vasodilator (NTG or ADO) was infused to normalize HBOC-201-induced increases in CBF. HBOC-201 had no effect on coronary blood flow (CBF) at rest and during exercise. HBOC-201 had no effect on mean arterial pressure (MAP) at rest and following HBOC-201 infusion.

Results: HBOC-201-induced increases in MAP were normalized by simultaneous NTG or adenosine (ADO) and NTG or ADO eliminated the effect. Exercise-induced increases in CBF were attributable primarily to increased heart rate; stroke volumes were essentially unchanged by ADO.

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Conclusions: HBOC-201-induced increases in MAP and PAP, MW and myocardial metabolism were abolished by HBOC-201, even during strenuous exercise. The HBOC-201-induced increases in MAP, MW and CBF can be prevented via simultaneous infusion of NTG or ADO.