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Arginine vasopressin during sinus rhythm: Effects on haemodynamic variables, left anterior descending coronary artery cross sectional area and cardiac index, before and after inhibition of NO-synthase, in pigs☆

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Summary We have shown previously that arginine vasopressin (AVP) given during sinus rhythm increases mean arterial blood pressure (MAP) and left anterior descending (LAD) coronary artery cross sectional area. AVP was assumed to result in vasodilatation via activation of the endothelial nitric oxide system. The purpose of the present study was to assess the effects of AVP before and after NO-inhibition.

Nine domestic pigs were instrumented for measurement of haemodynamic variables using micromanometer-tipped catheters, and measurement of LAD coronary artery cross sectional area employing intravascular ultrasound (IVUS). Haemodynamic variables, LAD coronary artery cross sectional area and cardiac

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output were measured at baseline, 90 s and 5, 15, and 30 min after AVP (0.4 U kg^{-1} IV) before and after blockade of nitric oxide synthase with N^G-nitro L-arginine methyl ester (L-NAME). Compared with baseline, AVP significantly increased MAP after 90 s (89 ± 4 versus 160 ± 5 mmHg), increased LAD coronary artery cross sectional area (11.3 ± 1 versus 11.8 ± 1 mm^2) and decreased cardiac index (138 ± 6 versus 53 ± 6 mL/min kg^{-1}). After blockade of nitric oxide synthase, AVP significantly increased MAP after 90 s (135 ± 4 versus 151 ± 3 mmHg), increased LAD coronary artery cross sectional area (8.7 ± 1 versus 8.9 ± 1 mm^2), and significantly decreased cardiac index (95 ± 6 versus 29 ± 4 mL/min kg^{-1}). IMPLICATIONS: During sinus rhythm, AVP increased MAP and LAD coronary artery cross sectional area, but decreased cardiac index.

Introduction

During cardiopulmonary resuscitation (CPR), arginine AVP has been shown to improve mean arterial blood pressure,[1] coronary perfusion pressure,[2] return of spontaneous circulation,[3] and 24-h survival rate.[4] However, concern has been raised that a substantial AVP-mediated increase in systemic vascular resistance may lead to myocardial depression.[5] Although previous CPR studies showed that AVP decreased coronary vascular resistance,[6] and increased LAD coronary artery cross sectional area, the CPR setting reflects autonomic insufficiency, therefore masking possible adverse AVP effects during normal sinus rhythm.[7] In fact, it is possible that AVP-mediated vasoconstriction in coronary arteries and subsequent myocardial ischemia were caused by excessive cumulative doses of AVP.[8,9] While AVP seemed to cause significant afterload complications in healthy patients, the exact mechanism appears unclear. For example, cardiac insufficiency could have been caused by excessive systemic vascular resistance, or direct AVP effects on the coronary arteries, or both. Moreover, the mechanism may be identified after blocking NO-receptors, because AVP was reported to produce coronary relaxation by activation of the endothelial nitric oxide system.[10] Thus, measurement of coronary artery cross sectional area and cardiac index after a AVP bolus injection before and after inhibition of NO-synthase may reveal better information about this phenomenon.

Accordingly, the purpose of the present study was to assess the effects of AVP on haemodynamic variables, coronary artery cross sectional area, and cardiac index during sinus rhythm, and the effects of AVP during inhibition of nitric oxide synthase with N^G-nitro L-arginine methyl ester (L-NAME). The null hypothesis was that AVP would have no effect on coronary artery cross sectional area and cardiac index.

Materials and methods

Surgical preparation and measurements

This investigation was approved by the Austrian Federal Animal Investigational Committee, and the animals were managed in accordance with American Physiological Society and institutional guidelines. Animal care and use was performed by qualified individuals, supervised by veterinarians, and all facilities and transportation comply with current legal requirements and guidelines. Anaesthesia was used in all surgical interventions, all unnecessary suffering was avoided, and research was terminated if unnecessary pain or fear resulted. This study was performed according to Utstein-style guidelines[11] on nine 12—16-week-old swine of either sex weighing 30—40 kg. The animals were fasted overnight, but had free access to water. One hour before surgery, the pigs were premedicated with azaperone (a neuroleptic agent; 4 mg kg^{-1} IM) and atropine (0.1 mg kg^{-1} IM). Anaesthesia was induced with a bolus dose of ketamine (20 mg kg^{-1} IM), propofol (1—2 mg kg^{-1} IV), and piritramid (30 mg IV) given via an ear vein.[12] The animals were placed on a U-shaped board, and their trachea was intubated during spontaneous respiration.

Thereafter, the animal's lungs were ventilated with a volume-controlled ventilator (Draeger EV-A, Lübeck, Germany) with 35% O_2 in 65% nitrous oxide at 15 breaths per minute, and with a tidal volume adjusted to maintain normocapnia. Anaesthesia was maintained with propofol (6—8 mg kg^{-1}/h) and piritramid IV as needed, muscle relaxation was provided with 8 mg pancuronium after intubation, and subsequently by a continuous infusion of pancuronium (0.2 mg kg^{-1}/h). Depth of anaesthesia was judged according to blood pressure, heart rate and clinical assessment. If cardiovascular variables indicated a reduced depth of anaesthesia, additional propofol and piritramid was given. Ringer's solution (6 mL kg^{-1}/h) and a 3% gelatine solution