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Basic Science Abstracts

Contents

A Cardiopulmonary Bypass Model in Rats

AUTHORS

Kawakami, Akiko[1]; Nakadate, Yosuke[1,2]; Omiya, Keisuke[1]; Oguchi, Takeshi[1]; Yamada, Mariko[2]; Matsukawa, Takashi[1]

[1] Department of Anesthesiology, University of Yamanashi, Chuo, Japan
[2] Department of Anesthesiology, University of Tsukuba Hospital, Tsukuba, Japan

INTRODUCTION

Cardiopulmonary bypass (CPB) is an essential technique in cardiovascular surgery. However, many adverse events have been reported with this circulation, such as the induction of inflammatory reactions and postoperative cognitive dysfunction, which affect patient outcomes. Animal experiments are useful for elucidating the mechanisms of adverse events and their prevention, and for developing new therapies. We describe a rat model suitable for studies using CPB.

METHODS

With Institutional Animal Investigation Committee approval, healthy male Sprague-Dawley rats were anesthetized with a nitrogen gas mixture containing 67% oxygen mixed with 3% isoflurane, and a 16-gauge intravenous catheter was used as an endotracheal tube. Following intubation, the rats were connected to a anesthesia machine (Fabius Tiro, Dräger) and ventilated with an inspiratory pressure of 15 cmH_2O, at a rate of 60 breaths/min, and with a positive end-expiratory pressure of 3 cmH_2O. After securing the airway, a 24-gauge intravenous catheter was inserted into the left femoral artery for arterial pressure measurement. The arterial line of CPB was secured with a 24-gauge intravenous catheter in the right femoral artery and a 17-gauge multi-orifice angiocatheter was inserted into the right external jugular vein as a venous line of the circuit. The CBP circuit was equipped with silicon tubes, a venous reservoir, a peristaltic pump and a membrane oxygenator with an effective membrane surface of 0.03 m^2 and primed with 6% hydroxyethyl starch, 7% sodium bicarbonate solution and heparin. The priming volume was 9 ml. Additional heparin was administered from the venous line or the reservoir to avoid membrane obstruction.

RESULTS

Without using any inotropic agents and blood transfusion, typical vital signs and arterial blood gas measurements at the end of 90 minutes extracorporeal circulation were the following: blood pressure 122/83 mmHg, heart rate 277 bpm, body temperature 33.2 ℃, pH 7.508, PaO_2 254 mmHg, $PaCO_2$ 32.5 mmHg, SaO_2 100%, Base Excess 3 mmol/L, HCO3 25.8 mmol//L Hb 8.2 g/dl, Hct 24%.

DISCUSSION

CPB model can be established in rats. This model is easy to assemble and does not need blood transfusion from additional rats. These are the advantages in terms of both costs and

animal ethics. This model has the potential to advance research in the field of cardiac anesthesia.

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No references

Bilateral Nephrectomy Impairs Cardiovascular Function and Cerebral Perfusion in a Rat Model of Acute Hemodilutional Anemia

AUTHORS

Jiang, Helen[1]; Chin, Kyle[1,2]; Liu, Elaine[1]; Steinberg, Benjamin E[2,3]; Goldenberg, Neil M[2,3]; Baker, Andrew J[1,4,5]; Connelly, Kim A;[2,6] Mazer, C David[1,2,5]; Hare, Gregory MT[1,2,4].

[1] Department of Anesthesiology and Pain Medicine, St Michael's Hospital, University of Toronto, ON, Canada
[2] Department of Physiology, University of Toronto, Toronto, ON, Canada
[3] Department of Anesthesia and Pain Medicine, The Hospital for Sick Children, The University of Toronto, Toronto, ON, Canada
[4] Keenan Research Centre for Biomedical Science in the Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, ON, Canada
[5] Institute of Medical Science, University of Toronto, Toronto, ON, Canada
[6] Division of Cardiology, Department of Medicine, University of Toronto, Toronto, ON, Canada

INTRODUCTION

Anemia is associated with acute kidney injury (AKI) and stroke in perioperative patients demonstrating potential vulnerability of these two organs during anemia. In addition, renal failure is an independent risk factor for perioperative stroke[1]. We wished to assess the physiological integration of renal oxygen sensing, increased cardiac output (CO) and maintained cerebral perfusion during acute anemia to determine the role of the kidney in maintaining cardiovascular responses to preserve brain perfusion during anemia. We performed acute bilateral nephrectomy (2Nx) to test the hypothesis that the kidney is required to maintain adequate cardiovascular responses to acute hemodilutional anemia and maintain brain perfusion and tissue oxygen tension.

METHODS

With Animal Care and Use Committee approval and in accordance with ARRIVE-2 guidelines, we performed sham or 2Nx on anesthetized (isoflurane 1.5%) Sprague-Dawley rats. Acute hemodilution was then performed by exchanging 50% estimated blood volume with hydroxyethyl starch (n=6-8 per group) over a ten minute period. Heart rate, mean arterial pressure (MAP), arterial blood gas (ABG), cooximetry and brain microvascular pO_2 (OxyLED, Oxyphor G4) were measured before and after acute hemodilutional anemia. In a separate experiment, CO and other left ventricular functions were measured by transthoracic echocardiography before and after acute hemodilution in 2Nx or sham operated rats (n=8 per group). Results were tested for normality and analysis performed by two-way ANOVA with $p<0.05$ as significant.

RESULTS

MAP was not different between groups before and after hemodilution. In sham animals, brain pO_2 remained stable at all times (32.5±4.2 mmHg). 2Nx resulted in a decrease in baseline brain pO_2 (21.1±2.9 mmHg, #; $P<0.001$) without impacting CO. Hemodilution of 2Nx

animals resulted in a further decrease in brain pO_2 (15.0±6.3 mmHg,*; P<0.001). 2Nx was associated with a small decrease in baseline diastolic and systolic left ventricular volumes (#; P<0.001), but no difference in CO. The CO response to hemodilution was attenuated in 2Nx animals, relative to sham rats (75±22 vs 108±19 mL/min, #; P<0.001); which was associated with a high systolic volume (156±51 vs 72±15 µL, #; P<0.001) and reduced stroke volume (223±66 vs 299±32 µL, #; P<0.001) relative to sham rats. This suggests that 2Nx impaired systolic function in response to anemia. ABG and cooximetry demonstrated comparable hemoglobin and blood oxygen content values between groups.

DISCUSSION

Control rats with normal renal function demonstrated a characteristic increase in CO following hemodilution which was associated with preserved brain perfusion (pO_2). 2Nx resulted in a reduction in baseline brain pO_2 with preserved CO, suggesting a possible impact of 2Nx on the cerebral vasculature. Following acute hemodilution, nephrectomy resulted in reduced systolic emptying and an attenuated CO response to acute anemia resulting in profound reduction in microvascular brain pO_2. These data support the hypothesis that renal oxygen sensing are required to initiate the increase in cardiac output required to maintain adequate cerebral perfusion during acute anemia. CAS-CARF support.

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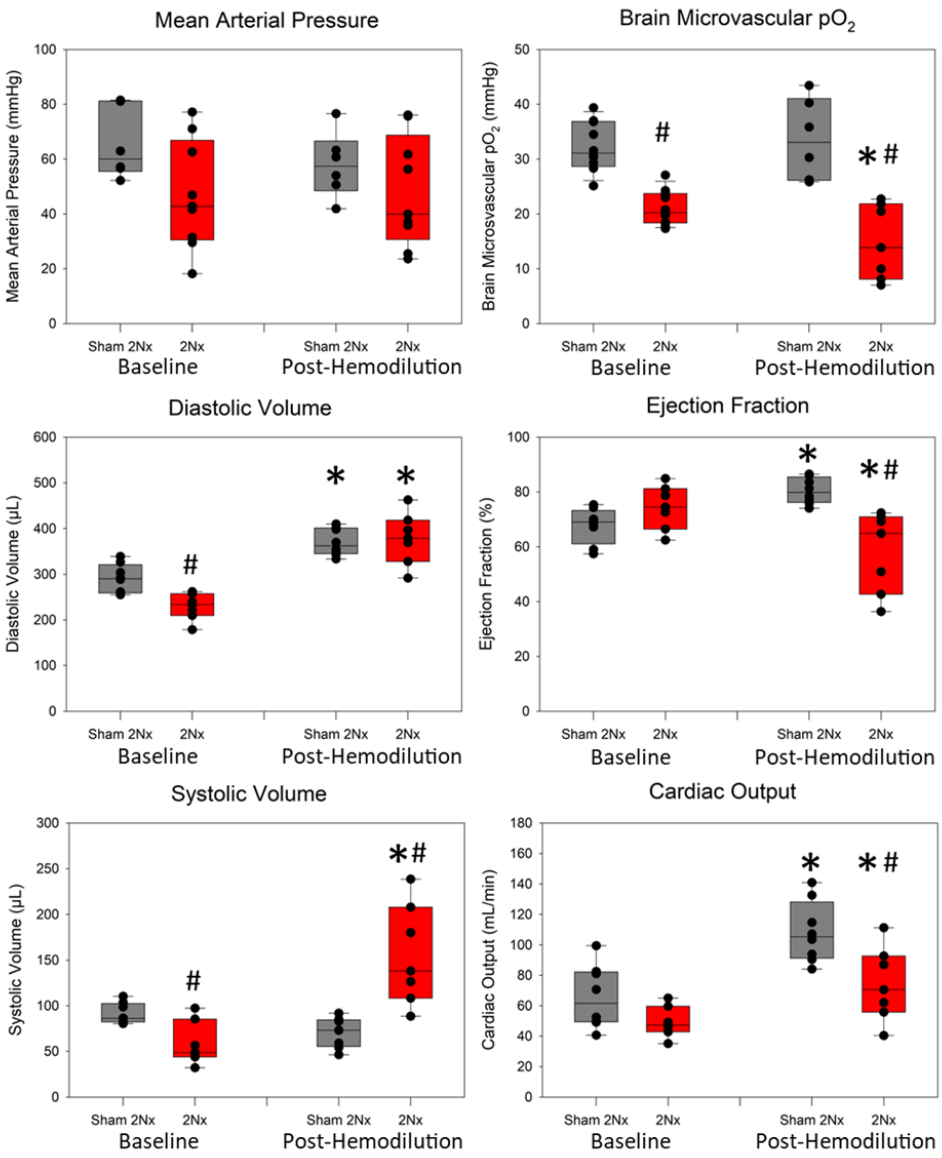
Mean Arterial Pressure
Mean Arterial Pressure (mmHg)
Brain Microvascular pO2
Brain Microvascular pO2 (mmHg)
Diastolic Volume
Diastolic Volume (µL)
Ejection Fraction
Ejection Fraction (%)
Systolic Volume
Systolic Volume (µL)
Cardiac Output
Cardiac Output (mL/min)
Sham 2Nx
2Nx
Baseline
Post-Hemodilution

Figure 1

The Cardioprotective Effects of S-equol for Myocardial Ischemia-Reperfusion Injury is Related to PI3K/Akt Pathway in the Experimental Animal Model

AUTHORS

Mariko, Yamada[1]; Yosuke, Nakadate[1,2]; Akiko, Kawakami[2]; Keisuke, Omiya[2]; Takeshi, Oguchi[2]; Makoto, Tanaka[1]; Takashi, Matsukawa[2]

[1] Department of Anesthesiology, University of Tsukuba, Tsukuba, Japan
[2] Department of Anesthesiology, University of Yamanashi, Chuo, Japan

INTRODUCTION

While S-equol, a metabolite derived from soy isoflavone, has protective effects on organs[1] through the phosphatidylinositol 3 kinase (PI3K)/Akt pathway[1], it is not fully understood whether it has beneficial effects against myocardial ischemia-reperfusion (IR) injury. Thus, we tested the hypothesis that S-equol has a cardioprotective effect against myocardial IR injury via the PI3K /Akt pathway, which plays important roles in IR injury. The primary outcome was maximum left ventricular pressure derivative (LV dP/dt max) 20 min after reperfusion.

METHODS

After approval from the Institutional Animal Investigation Committee, 32 hearts were excised from male Wistar rats (weighing 300-320 g) under anesthesia. The hearts were perfused with the Langendorff system at a constant pressure, with modified Krebs-Henseleit (KH) buffer. The LV was cannulated with a thin latex balloon for continuous monitoring of LV pressure. To assess the relationship between the cardioprotective effects of S-equol and PI3K/Akt, an inhibitor of PI3K (wortmannin) was used. The rats were randomly divided into four groups: 1) Control group (Cont): KH buffer, 2) Control and wortmannin group (ContW): wortmannin 100 nmol/L in KH buffer, 3) S-equol group (EQ): 1 μmol/L S-equol, 4) S-equol and wortmannin group (EQW): 1 μmol/L S-equol and wortmannin 100 nmol/L in KH buffer. The hearts were perfused with each perfusate for 20 min prior to 7.5 min of no-flow ischemia with pacing followed by 20 min of reperfusion. LV dp/dt max were recorded at baseline, pre-ischemia, and at 5, 10, 15, and 20 min after reperfusion. Muscle sampling was performed after 20 min of reperfusion to measure phosphorylated Akt (pAkt) by Western blotting.
Hemodynamic data and pAkt were analyzed with two-way and one-way ANOVA followed by Bonferroni test, respectively.

RESULTS

Baseline measurements were similar among four groups. The LV dp/dt max in the EQ group at 15 and 20 min after reperfusion was significantly higher than that of the Cont group(742±468 vs 249±304, $p=0.012$, 1020±607 vs 299±348, $p<0.001$, respectively), and this effect was diminished by wortmannin (Fig). In western blotting, the myocardial pAkt level in the EQ group was significantly increased compared to that in the Cont group ($p=0.036$).

DISCUSSION

S-equol exerted a cardioprotective effect against myocardial IR injury probably due to the PI3K/Akt signaling activation considering our results that cardiac contractility in EQ group recovered better than control group and diminished in the presence of PI3K inhibitor after IR injury. Myocardial pAkt elevation observed in EQ group also support our hypothesis. Further study is needed to apply clinical cardiac anesthetic setting.

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