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BRIEF COMMUNICATION

Cardiopulmonary bypass model in the rat: a new minimal invasive model with a low flow volume†

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Abstract

Numerous cardiopulmonary bypass (CPB) models in the rat have already been described, but these models often have an important mortality and differ a lot from human clinical conditions thus making them hardly usable.

The CPB model in the rat we describe allows a femoro-femoral support CPB with a low priming volume, minimal surgical approach and excellent peroperative survival. This CPB model in the rat allows evaluating extracorporeal circulation effects.

Keywords: Cardiopulmonary bypass • Experimental surgery • Animal model

INTRODUCTION

Numerous CPB models in the rat have already been described [1–7] with various cannulation sites, circuits, priming volumes (12–120 ml), products used for priming, temperature and outflows. Often, these models differ from human clinical conditions thus making them hardly usable.

We here describe a model allowing a femoro-femoral support CPB with a low priming volume, minimal surgical approach and excellent peroperative survival.

TECHNIQUE

This CPB model was performed in Wistar male rats (450–500 g), divided into two groups of 10 rats each (Sham group, femoral cannulation without CPB and CPB group, femoral cannulation with CPB). All rats were housed in individual cages and received care in accordance with the 'Guide for the Care and Use of Laboratory Animals' (www.nap.edu/catalog/5140.html).

Extracorporeal circulation (Fig. 1)

We use a 16 G catheter (Introcan Safety BRAUN®) as a venous cannula and a 22 G one as an arterial cannula. Arterial and venous tubings as well as the pump are in PVC (internal diameter: 2.5 mm. length = 20 cm). 'Cardiotomy' reservoir is made of a sterile 5 ml syringe (TERUMO®) connected to two consecutive 3-way taps, screwed to the pump. We use an occlusive roller pump (GAMBRO®).

The oxygenator is a 'Micro 1' (Kewei Medical Instrument Inc, Shenzhen, China) with a 0.05 m^2 exchange surface which has already been the subject of several publications [5–7] validating its oxygenation capacities. The circuit is aseptically set-up and 'freed of air bubbles' with Gelofusine® at 4% (BRAUN). Circuit priming volume is 10 ml (Gelofusine® 4%).

Operative protocol

After anaesthesia (intra-peritoneal injection of Chlorpromazine Chlorhydrate (2 mg/kg) and Ketamine (80 mg/kg)), a heparinized 3F catheter is introduced into the left carotid. This approach is used as an injection access and allows for a continuous pressure monitoring. Heparin (500 UI/kg) and pancuronium bromide (1 mg/kg) are injected through this access.

After orotracheal intubation (Arkansas no.18 cannula), continuous mechanical ventilator support is set-up at a 75 cycles/min rate, a 10 ml/kg circulating volume and a 100% FiO_2 outside CPB (21% during CPB). Further to intubation, a pancuronium bromide injection is achieved through the left carotid.

The femoral vein is cannulated with a 16G catheter, and the artery with a 22G catheter. The rat is placed upon a hotplate with a 30° proclive positioning to ease venous drainage.

In the CPB group, cannulae are connected to the circuit after a 2 ml Gelofusine® filling. CPB outflow is progressively increased to 100 ml/kg/min. Vascular filling is achieved with Gelofusine®, in compensation for diuresis, in order to maintain a MAP ≥ 70 mmHg and an adequate venous drainage for CPB. Rats not subjected to CPB (sham group) were monitored for 150 min after cannulation before being sacrificed.

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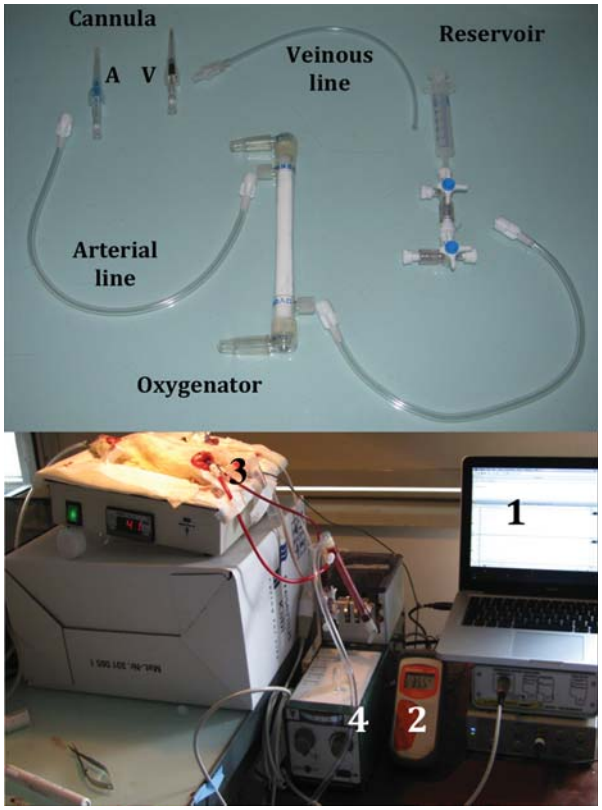

Figure 1: The cardiopulmonary bypass circuit and its monitoring. 1, blood pressure and electrocardiogram; 2, temperature; 3, diuresis; 4, CPB flow pump.

During the entire experiment, tensional, rhythm, thermal and diuresis monitoring were performed (Fig. 1). Diuresis was measured with a graded collector set against the urinary meatus. Breathing and oxygenator parameters (O_2 outflow) were adjusted according to gasometry so as to obtain a pH = 7.35, a PaO_2 = 30 KPa and a $PaCO_2$ = 5 KPa. Arterial gasometry monitoring was performed 20 min after femoral canulation and then after every breathing parameter modification and at CPB discontinuation.

Blood samples (2 ml) were collected at cannulation (T0) and at the time of sacrifice of the rats (T1 = T0 + 150 min), and immediately centrifuged at 500 × g. Plasma samples were stored at −80°C for measurement of serum tumour necrosis factor (TNF)-α using an ultrasensitive kit specific for rat TNF-α (Cytoscreen; Biosource International, USA). The assay was performed by measuring optical density at 450 nm. Each sample was measured in duplicate and compared with a known concentration range of TNF-α. The limit of detection was 0.7 pg/ml.

The rats were euthanized at the end of the study.

Data analysis

All results are presented with a mean ± standard deviation. Results were compared with the Student's *t*-test. A $P < 0.05$ value is considered as statistically significant. Statistical analysis was performed with Statview® computer program.

RESULTS

None of the rats died during the procedure.

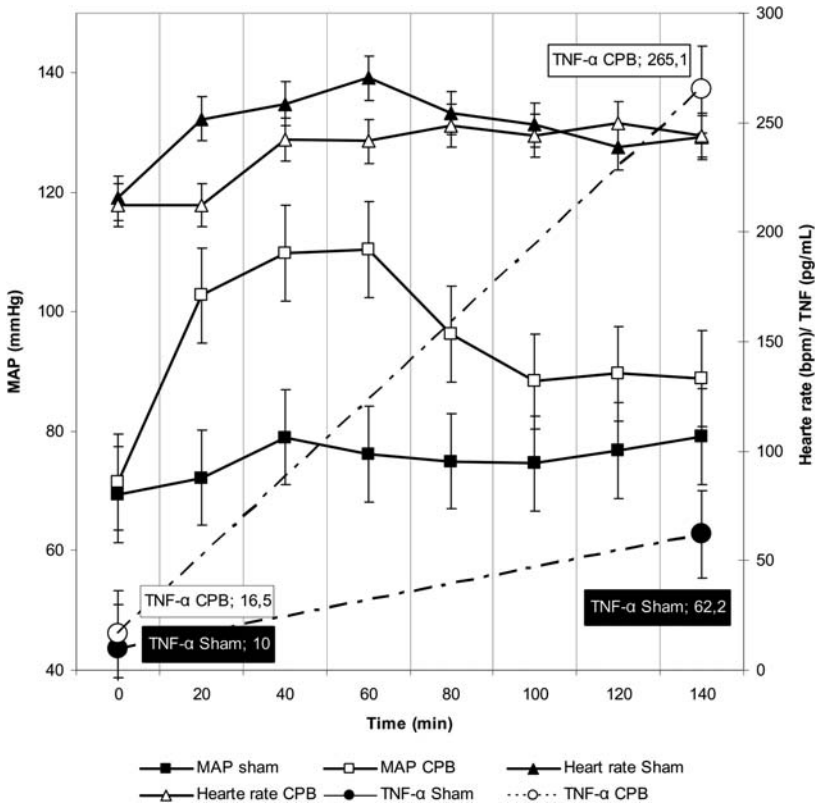

Figure 2: Blood pressure, heart rate and TNF-α values during the procedure.

Mean arterial pressure analysis during the experiment (Fig. 2) reveals a higher MAP ($P < 0.0001$) at post-cannulation 20th, 40th and 60th min in the CPB group compared with the sham group. Observed heart rates do not significantly vary between the two groups. Vascular filling and diuresis are significant ($P < 0.0001$) in the CPB group.

TNF-α values (Fig. 2) at T1 are significantly higher in the CPB group ($P < 0.0001$), and above those measured at T0 for both groups in which they are very low.

DISCUSSION

Studying inflammation process requires reduced surgical aggression, which led us to use a femoral cannulation (closed chest). Consequently, the observed inflammatory response is induced by the one caused by blood contact with CPB circuit. Indeed, in human clinical evaluation, the role played by the surgical trauma in complement activation has been well established [8]. In our model, it was mild.

Furthermore, our model offers the advantage of a low priming volume not requiring transfusion and without raising the issue of venous drainage. To avoid this problem, we used rats weighing between 450 and 500 g (larger volemia). Besides, diuresis monitoring enables compensating it with the inflow. Lastly, placing the rat in a 30° proclive position 15 cm above cardiotomy reservoir level improves venous drainage and a stable 100 ml/kg/min CPB output is obtained.

Since it is a circulatory assistance without cardiac arrest, we observe increased mean pressures during extracorporeal circulation. MAP difference after CPB is probably due to the filling variation between the control and the CPB groups, as well as to the returned part of circuit volume at the end of CPB.

CONCLUSION

This CPB model in the rat allows evaluating extracorporeal circulation effects. It has the advantages of CPB circuit low volume, peripheral cannulation and reduced surgical aggression together with low mortality.

Conflict of interest: none declared.

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