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Simultaneous measurement of arterial and left ventricular pressure in conscious freely moving rats by telemetry

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ABSTRACT

Comprehensive cardiovascular assessment in conscious rodents by utilizing telemetry has been limited by the restriction of current devices to one pressure channel. The purpose of this study was to test and validate a dual pressure transmitter that allows the simultaneous measurement of arterial pressure (AP) and left ventricular pressure (LVP) in conscious freely moving rats. Six rats were surgically implanted with dual pressure transmitters. Baseline hemodynamics and circadian rhythm were observed to return within 7 days. AP, heart rate (HR), LVP and indices of left ventricular contractility were stable and demonstrated a prominent circadian rhythm over a two-week period of uninterrupted recordings. Administration of the vasodilator nifedipine produced the anticipated dose-dependent decrease in AP which was accompanied by a baroreflex mediated increase in HR and cardiac contractility. The negative inotrope verapamil produced the expected dose-dependent decreases in AP and cardiac contractility. Finally, a terminal validation of the dual pressure transmitter was performed under anesthesia by measuring AP and LVP simultaneously via telemetry and from a fluid filled arterial catheter and an intraventricular Millar catheter, respectively. A range of pressures and cardiac contractility were studied by administering sequential intravenous infusions of the positive inotrope dobutamine followed by verapamil. Linear regression analysis revealed a high level of agreement between pressures measured by the dual pressure transmitter and the exteriorized catheters. Histopathologic analysis of the heart revealed mild peri-catheter fibrosis. In conclusion, the simultaneous measurement of AP and LVP offers the potential for more detailed cardiovascular assessment in conscious rats.

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1. Introduction

The measurement of cardiovascular (CV) parameters in small laboratory animals by telemetry has become an integral part of cardiovascular research. Telemetry enables the continuous, long-term recording of physiological variables in conscious, undisturbed animals. This provides precise measurements while avoiding stress artifacts inherent with the use of physical or chemical restraint (Kramer & Kinter, 2003; Kramer & Remie, 2005). Although selection of the measurement technique should always be driven by the study objective, telemetry is now recognized as the preferred method to chronically monitor cardiovascular responses in the research laboratory (Kurtz, Griffin, Bidani, Davisson, & Hall, 2005). The most frequent application of telemetry in cardiovascular research has been in the monitoring of pressure signals, in particular the measurement of arterial blood pressure in rats (Handoko et al., 2008; Hess, Clozel, & Clozel, 1996).

A significant limitation in the application of telemetry in small animals has been the technological restriction of current telemetry devices to one pressure channel. As a result, the simultaneous measurement of two pressure signals in the same small animal to provide a more comprehensive cardiovascular characterization has not been possible. The simultaneous monitoring of arterial (AP) and left ventricular pressure (LVP) to assess peripheral hemodynamics along with measures of cardiac contractility in the same conscious animal would provide a more thorough integrated cardiovascular assessment in response to an intervention. The purpose of this study was to describe and validate a new method that allows the simultaneous measurement of arterial pressure and left ventricular pressure in conscious freely moving rats by telemetry. We demonstrate that chronic measurements of arterial pressure and left ventricular pressure, along with recordings of the electrocardiogram and core body temperature can be successfully performed in the same rat and are stable over time. In addition, there was a high level of agreement between arterial and left ventricular pressures measured by telemetry and those measured by acutely implanted exteriorized catheters in a terminal validation study.

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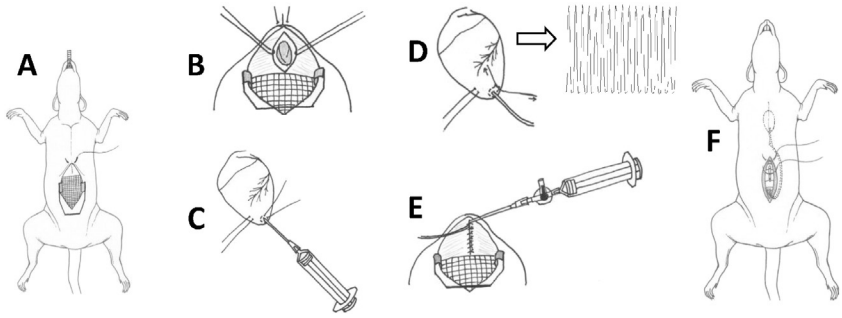

Fig. 1. Visual representation of the trans-diaphragmatic insertion of a HD-S21 telemetry catheter into the apex of the left ventricle. A. positioning of anesthetized animal; B. Visualization of the heart through diaphragm; C. Piercing of left ventricle; D. Insertion of catheter with signal validation; E. Diaphragm closure; F. Closure of abdomen.

2. Methods

2.1. Animals

All protocols were approved by the Abbvie Institutional Animal Care and Use Committee and performed in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals. All animals were housed under standard laboratory conditions with a 12 h light/dark cycle, in a temperature and humidity controlled room with free access to standard rodent diet and water. Six male Sprague–Dawley rats (Charles River Laboratories, Portage, MI) weighing approximately 300 g at the beginning of the study were used.

2.2. Surgical instrumentation

2.2.1. General anesthesia and surgical preparation

General anesthesia was induced in an anesthesia induction chamber with a mixture of 2–4% isoflurane (Hospira, Lake Forrest, IL) in oxygen. Tracheal intubation was performed with laryngoscope guidance using tapered PE240 tubing connected to a rodent ventilator. General anesthesia was maintained by delivering a mixture of 0.5–2.0% isoflurane in oxygen by mechanical ventilation (breathing frequency 80/min, pressure 9/0 cm H_2O, inspiratory/expiratory ratio 1:1). Surgical plane anesthesia was maintained for the duration of the surgery and rats were closely monitored for the depth of anesthesia. The rat was paced on a heated surgical field in dorsal recumbency. The hair over the ventral abdomen and thorax was shaved and the skin was surgically prepared with Duraprep (3 M, Minneapolis, MN). The surgical site was then draped with sterile gauze.

2.2.2. Surgical procedure

All surgeries were performed by a ventral midline laparotomy using aseptic technique. A 5-cm ventral midline abdominal incision beginning just caudal to the xiphoid process was made. The abdominal organs were covered with gauze soaked in warm sterile saline. A 3-0 nylon suture was inserted through the xiphoid and retracted anteriorly to lift the thoracic cavity to allow maximum exposure of the diaphragm (Fig. 1A). A midline vertical incision was made in the diaphragm and a 5-0 propylene suture passes through each side to retract the diaphragm and expose the heart (Fig. 1B). The pericardium was then opened and a shallow 5-0 silk suture was placed in the right ventricle of the heart to retract and expose the left ventricle of the heart. A purse string suture using 5-0 silk was placed in the apex of the left ventricle. The left ventricle was punctured through the purse string suture with a 20 G needle and the tip of one of the telemetry pressure catheters was inserted into the ventricle up to the suture rib (approx. 8 mm) (Fig. 1C). The

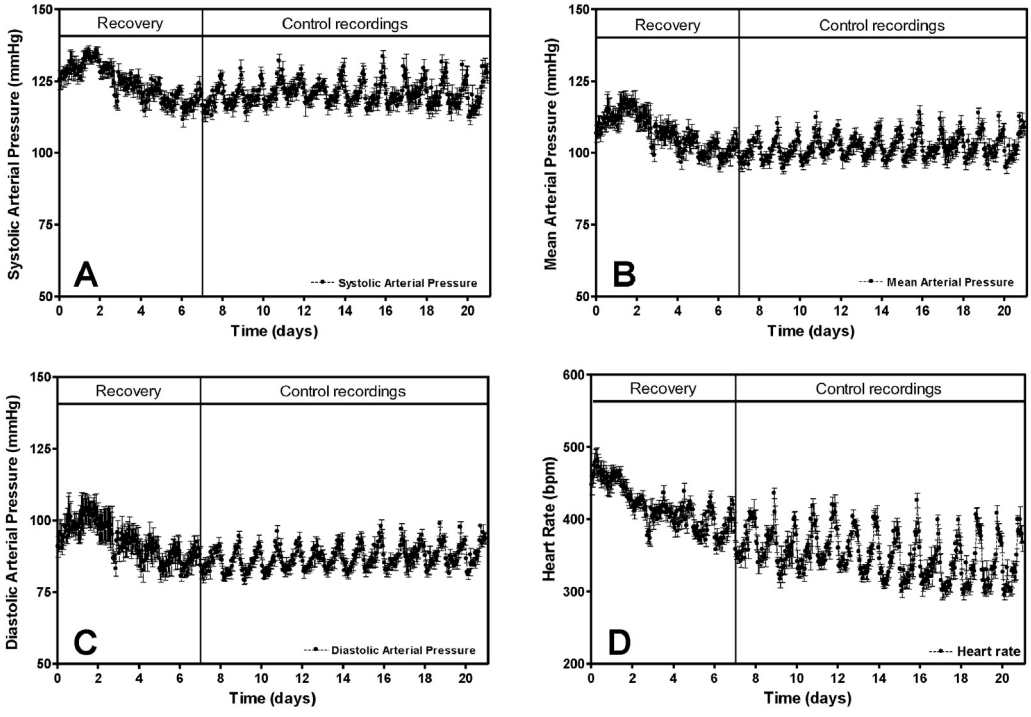

Fig. 2. Baseline hemodynamics observed for 21-days immediately following surgery. A: systolic arterial pressure, B: mean arterial pressure, C: diastolic arterial pressure, D: heart rate.

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