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Simultaneous Pulmonary and Systemic Blood Pressure and ECG Interval Measurement in Conscious, Freely Moving Rats

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Here we evaluated the ability of a new, dual blood-pressure telemetry transmitter to simultaneously measure pulmonary and systemic blood pressure and the electrocardiogram in rats. The transmitter was implanted in normotensive and monocrotaline-induced pulmonary hypertensive Wistar rats, with sensing catheters placed in the pulmonary artery (channel 1) and descending aorta (channel 2). Biopotential electrodes were positioned to record an apex-based lead II electrocardiogram. Pulmonary and systemic arterial blood pressure and electrocardiographic waveforms were recorded between 2 and 12 wk after implantation of the transmitter. During this period, pulmonary arterial pressure progressively increased in monocrotaline-treated compared with saline-treated rats. The pharmacologic response of rats to reference compounds was measured by using the transmitter to validate the technique and to evaluate the ability of the device to transmit changes in blood pressure and the electrocardiogram. Validation against 2 Millar high-fidelity blood-pressure catheters confirmed the accuracy of the blood pressure data recorded with the transmitter. In addition, local tolerance of the associated catheters was confirmed by histologic examination.

Abbreviations: MAP, mean arterial pressure; MPAP, mean pulmonary arterial pressure.

Few long-term monitoring systems are available for dual pulmonary and systemic blood pressure measurement in freely moving small animals. Until now, only systemic or pulmonary arterial blood pressure, but not both, could be recorded in a single conscious rat.[2,7] The ability to simultaneously collect 2 blood pressures, heart rate, and electrocardiographic intervals in a conscious animal without interference of anesthesia and stress due to manipulation would be a great improvement in experimental capabilities. In addition, this advance would reduce interanimal variability associated with collecting single pressures from 2 different animals and decrease the number of animals required by half.

Here we evaluate the use of a new, small-animal dual blood-pressure telemetry transmitter to record pulmonary and systemic blood pressure and electrocardiogram in individual, freely moving rats. To evaluate this system, we used monocrotaline to induce pulmonary hypertension in rats. Injection of monocrotaline causes morphologic damage that leads to the development of lesions that are similar to those in humans with primary pulmonary hypertension.[5,8-10] Previously, simultaneous assessment of pulmonary and systemic arterial blood pressure in monocrotaline-treated rats was possible only with an invasive method and anesthesia.[11]

We used the dual blood-pressure transmitter to measure the pharmacologic response of naïve and pulmonary hypertensive rats to reference compounds to validate the technique and to evaluate the ability of the device to transmit changes in blood pressures and electrocardiographic traces. Because oral endothelin receptor antagonists are clinically and experimentally efficacious in the treatment of pulmonary hypertension,[3,4,12] we here used one of these agents to decrease pulmonary arterial blood pressure. Similarly, we also included verapamil, a calcium channel blocker used to lower systemic blood pressure in normotensive and hypertensive animal models.[1,6] To confirm the accuracy of the blood pressure data recorded by using the dual-pressure transmitter, we compared these data with pulmonary and systemic blood pressure values obtained with 2 Millar high-fidelity catheters. We assessed the local tissue tolerance of the catheters in the dual-pressure system through histologic examination.

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Materials and Methods

Animals. Normotensive male Wistar rats (n = 13; weight on day of surgery, 257 to 276 g) were obtained from Harlan Laboratories (Horst, The Netherlands), group-housed during a 2-wk acclimation period, and individually caged after implantation of the telemetry device. Single rats were housed in polycarbonate cages (Makrolon III, Eurostandard H, Tecniplast, Varase, Italy) with wire-mesh tops, standardized softwood bedding (LTE E-001 Aspen Sawdust, Abedd, Vienna, Austria), and appropriate environmental enrichment (polycarbonate rat tunnel and aspen bricks, Datesand, Manchester, UK). All rats were maintained under identical conditions and had free access to drinking water and pelleted food (no. 3336, Provimi Kliba, Kaiseraugst, Switzerland), under climate-controlled conditions (18 to 22 °C, 40% to 60% relative humidity), with a 12:12-h light:dark cycle in accordance with the guidelines of the Baselland Cantonal Veterinary Office (license no. 185).

Surgical procedure. After the acclimation period, 8 rats were weighed and pretreated with buprenorphine (0.03 mg/kg SC, Essex Chemie, Luzern, Switzerland) and enrofloxacin (15 mg/kg, Baytril 2.5%, Bayer, Provet, Lyssach, Switzerland). Anesthesia was induced and maintained through inhalation of 2.5% isoflurane (70% air, 30% O_2; Garbagas, Basel, Switzerland).

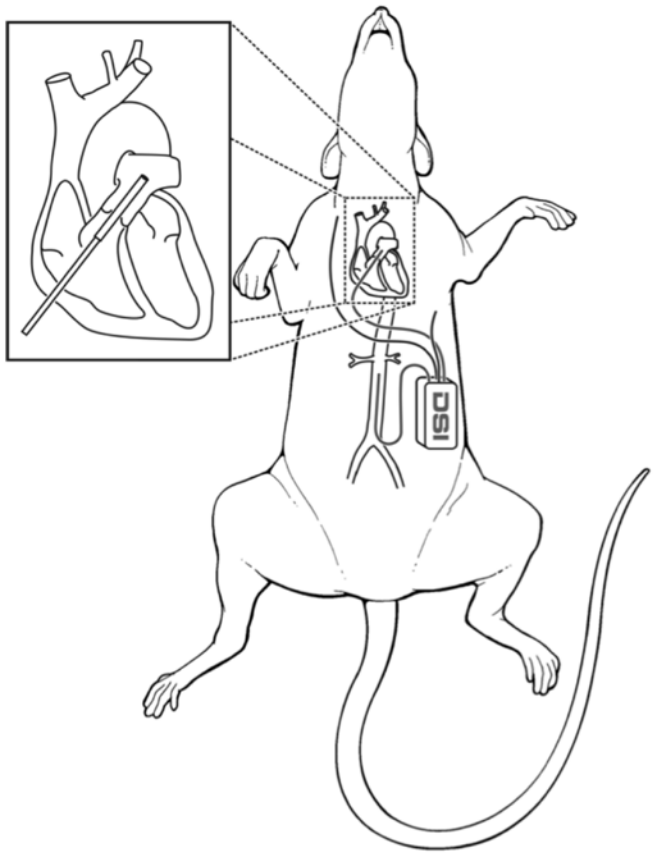

Figure 1. Location of the dual-pressure telemetry transmitter on the experimental animal. Figure courtesy of Data Sciences International.

A drop of ophthalmic lubricant (Viscotears, Novartis, Bern, Switzerland) was applied to each eye. The rats were intubated orotracheally (outer diameter, 2 mm), and the lungs were ventilated mechanically (60 cycles per minute; tidal volume, 6 to 9 mL; KTR5 Small-Animal Ventilator, Hugo Sachs Elektronik–Harvard Apparatus, March–Hugstetten, Germany). Under sterile conditions, the abdomen was opened with a midline abdominal laparotomy, and the thorax was opened by a right lateral thoracotomy at the sixth to seventh intercostal space. By using a stainless steel trocar, a trench was made from the peritoneal cavity, through the external oblique musculature and intercostal space, and into the thorax. The dual blood-pressure transmitter (HD-S21, Data Sciences International, St Paul, MN) was placed in the abdominal cavity, and the channel-1 sensing catheter was positioned in the thorax by using the trocar. After removal of the trocar, the right ventricle was exposed and punctured with an 18-gauge needle (Microlance 3, Becton Dickinson, Drogheda, Ireland). The sensing catheter was inserted into the right ventricle through this small hole and pushed into the pulmonary artery. During diastole, the trace from the catheter drops to almost 0 mm Hg in the right ventricle and increases to roughly 15 mm Hg when it enters the pulmonary artery. The traces were monitored continuously during the entire surgical intervention. After appropriate placement of the tip of the sensing catheter in the pulmonary artery, the catheter was fixed on the right ventricle by using 6-0 polypropylene nonabsorbable suture (Prolene, Ethicon, Johnson and Johnson, Spreitenbach, Switzerland). The chest was closed with 4-0 polyglactin 910 absorbable suture (Vicryl, Ethicon, Johnson and Johnson), and the vacuum in the thorax was reestablished by using a 10-mL syringe. Bipolar electrodes were implanted to record a

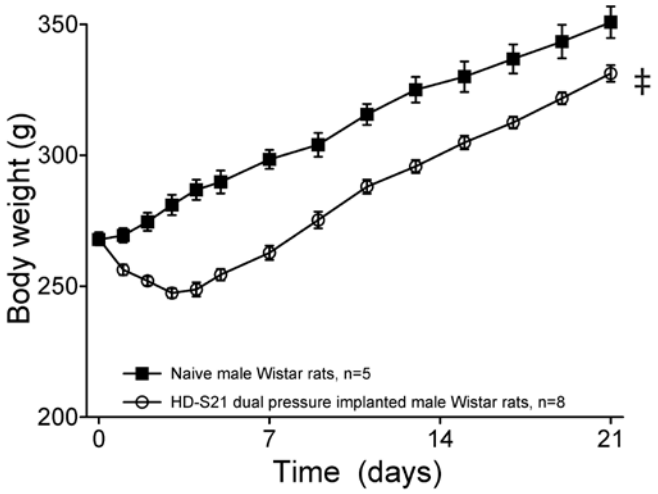

Figure 2. Body weight (g; mean ± SEM) after implantation of the dual-pressure telemetry transmitter in male Wistar rats. ‡, $P < 0.001$ at 3 wk compared with baseline values.

lead II apex-to-base electrocardiogram (right thoracic ventral serratus muscle to external oblique abdominal muscle). The channel-2sensing catheter was placed in the descending aorta below the renal arteries, pointing upstream. The catheter was secured in place by using a cellulose patch and medical tissue adhesive (no. 1469 SB, Vetbond, 3M Health Care, St Paul, MN). By using nonabsorbable suture (4-0 Dagrofil, B Braun, Aesculap, Tuttlingen, Germany), the transmitter was sutured to the inside of the abdominal wall, 1 cm from the edge of the incision (Figure 1). The electrocardiographic electrodes were fixed 4-0 Dagrofil (B Braun, Aesculap), the abdominal muscular layer was closed with 4-0 Vicryl (Ethicon, Johnson and Johnson), and the dermis was closed with medical tissue adhesive and disposable skin staple (DS15, Precise, 3M Health Care). During recovery from anesthesia, the rats were extubated, transferred into a dedicated recovery room, and monitored for 4 d. Buprenorphine (0.03 mg/kg SC) was administered once daily for 4 d after surgery.

Telemetry system and data collection. The dual blood-pressure transmitter (diameter, 0.7 mm; catheter length, 10 cm; weight, 8 g ; volume, 5.9 mL; Data Sciences International) was designed to measure 2 arterial blood pressures, electrocardiographic traces, body temperature, and locomotor activity. Implants were sterilized and provided precalibrated (relative to a vacuum) by the manufacturer. Before implantation, transmitter calibration was verified at room temperature to be accurate within 3 mm Hg. The transmitter digitally sent calibration and serial number information to a receiver (RPC1, Data Sciences International) during configuration. The signal from the receiver was consolidated by a multiplexer (Data Exchange Matrix, Data Sciences International) and was sent to a designated personal computer (Optiplex 960, Dell, Dublin, Ireland). Arterial pressures were normalized by using input from an ambient pressure reference (APR1, Data Sciences International). Blood pressure and electrocardiographic data were collected continuously (version 4.3, Dataquest ART Gold, Data Sciences International). Arterial pressure signals were sampled at 500 Hz. Systolic arterial pressure, mean arterial pressure (MAP), diastolic arterial pressure, and heart rate for systemic and pulmonary arterial pressure were collected at 5-min intervals for 24 h, resulting in a series of 2304 data points for each rat. Hourly arterial blood pressure means were calculated. Electrocardiographic signals were sampled at 1000 Hz; waveforms were collected for 10 s at 5-min intervals.

Table 1. Measurement of pulmonary and systemic blood pressure and heart rate after implantation of the dual blood-pressure telemetry transmitter in male Wistar rats (n = 4 per group) treated with a single dose of saline (3 mL/kg) or monocrotaline (60 mg/kg) at week 3

		Arterial pressure (mm Hg)						
Treatment	Time (wk) after implantation	Systolic	Mean	Diastolic	Systolic pulmonary	Mean pulmonary	Diastolic pulmonary	Heart rate (bpm)
Saline	2	127 ± 1	107 ± 1	89 ± 1	28 ± 1	22 ± 1	17 ± 1	391 ± 4
	3	128 ± 1	108 ± 1	90 ± 1	29 ± 1	22 ± 1	16 ± 0	387 ± 5
	4	128 ± 2	108 ± 2	91 ± 2	28 ± 0	21 ± 1	14 ± 2	380 ± 2
	5	127 ± 1	107 ± 1	91 ± 1	28 ± 1	21 ± 1	14 ± 2	372 ± 3
	6	130 ± 2	110 ± 2	92 ± 1	27 ± 1	21 ± 1	15 ± 0	371 ± 5
	7	128 ± 2	108 ± 2	91 ± 1	27 ± 1	20 ± 1	14 ± 0	368 ± 5
	8	129 ± 1	109 ± 1	93 ± 2	26 ± 1	20 ± 1	13 ± 0	360 ± 6
Monocrotaline	2	129 ± 1	109 ± 1	90 ± 0	28 ± 1	22 ± 0	17 ± 0	400 ± 5
	3	130 ± 2	110 ± 2	92 ± 1	29 ± 1	22 ± 0	17 ± 0	392 ± 6
	4	129 ± 2	109 ± 2	91 ± 1	28 ± 1	22 ± 1	16 ± 1	380 ± 7
	5	129 ± 2	109 ± 1	92 ± 1	30 ± 1	23 ± 1	17 ± 1	372 ± 4
	6	132 ± 2	111 ± 1	93 ± 1	46 ± 12	33 ± 7	22 ± 3	376 ± 6
	7	127 ± 4	108 ± 3	91 ± 1	58 ± 15	39 ± 8	24 ± 4	381 ± 11
	8	128 ± 4	108 ± 3	91 ± 2	54 ± 14	36 ± 8	21 ± 4	368 ± 4

There was no statistical difference between values obtained from monocrotaline-treated compared with vehicle-treated rats.

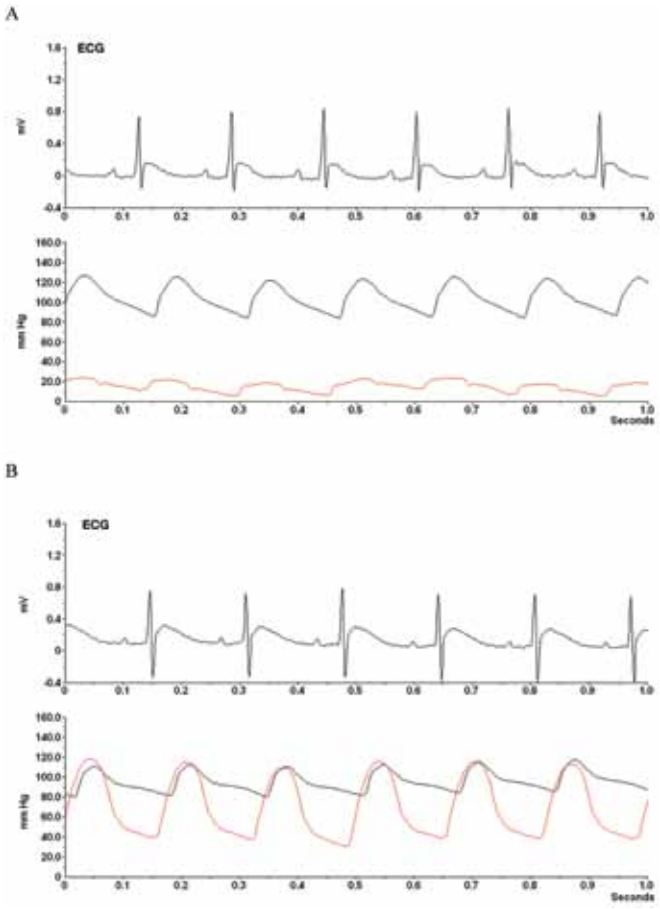

Figure 3. Systemic arterial blood pressure, pulmonary arterial blood pressure and electrocardiographic intervals in a conscious freely moving male Wistar rat. (A) 3 wk after implantation of the transmitter. (B) 9 wk after implantation of the transmitter (6 wk after monocrotaline injection). Traces demonstrate a lead II apex-based electrocardiogram and systemic (black line) and pulmonary (red line) arterial blood pressure signals over 1 s.

Experimental design. The first part of the study evaluated the postsurgical recovery, body weight, and systemic and pulmonary pressure during the 8 wk immediately after implantation of the telemetry transmitter and development of pulmonary arterial hypertension. In the second part of the study (weeks 9 through 11 after surgery), systemic and pulmonary arterial pressure and electrocardiographic responses to pharmacologic reference compounds were measured (crossover design) to validate the technique and to evaluate the ability of the transmitter to accurately and reliably transmit changes in blood pressure and electrocardiographic traces. All hemodynamic baseline parameters before treatment were the same between experimental groups. In the third part of the study (week 12 after surgery), the systemic and pulmonary artery pressure signal traces obtained by using the dual-pressure transmitter were validated and compared with those from a 2-French high-fidelity Millar blood pressure transducer (model SPR407, Millar Instruments, Houston, TX). The reliability of the electrocardiographic waveform quality obtained by using the dual-pressure transmitter was compared with that recorded by using an EMKA PowerLab (IOX, EMKA Technologies, Paris, France). Finally, local tolerance of the associated catheters in target organs was determined by histologic examination.

At 3 wk after transmitter implantation, rats were randomized according to blood pressure and body weight into 2 test groups (n = 4 per group). A single dose of monocrotaline (60 mg/kg SC; total volume, 3 mL/kg; Sigma Chemicals, St Louis, MO) was administered to each rat in the treatment group to induce pulmonary arterial hypertension. Rats in the control group each received a single subcutaneous injection of 9 g/L NaCl (total volume, 3 mL/kg).

An endothelin receptor antagonist (10 mg/kg PO; Actelion Pharmaceuticals, Allschwil, Switzerland) was used to reduce pulmonary arterial blood pressure. The calcium-channel blocker verapamil (30 mg/kg PO; verapamil hydrochloride, Fluka Chemie, Buchs, Switzerland) was used to lower systemic arterial blood pressure. Purified water and gelatin 7.5% were used as the vehicle. The oral administration volume was 5 mL/kg. All experiments were performed in a crossover design; all rats

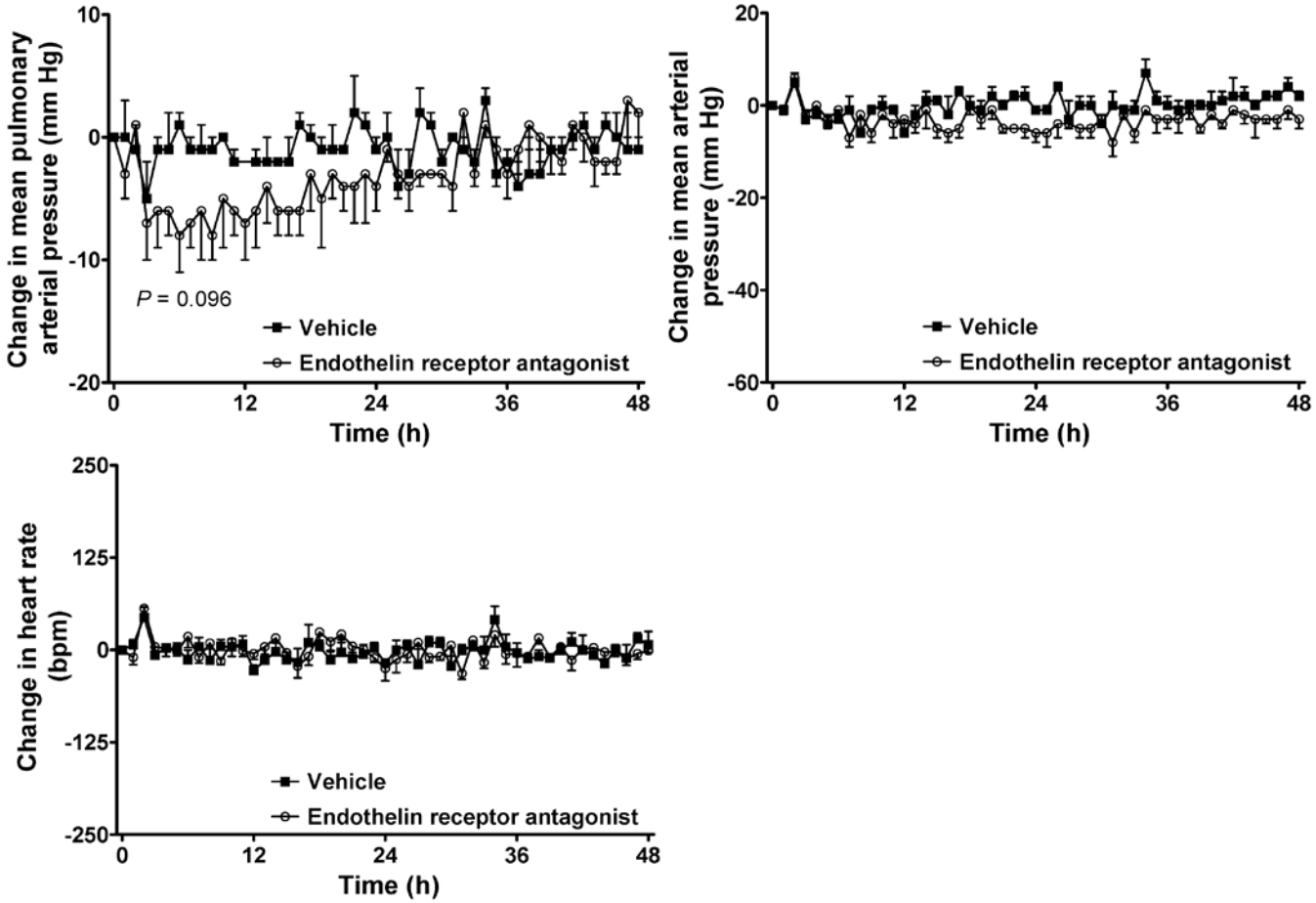

Figure 4. Effect of single oral administration of endothelin receptor antagonist (10 mg/kg PO) on mean pulmonary arterial pressure, mean arterial pressure, and heart rate in conscious, freely moving pulmonary hypertensive Wistar rats (n = 4). Data are presented as change in hourly mean ± SEM. Maximal decrease in mean pulmonary arterial pressure was obtained 6 h after oral administration (P = 0.096).

received endothelin receptor antagonist, verapamil, and vehicle, with a 7-d washout period between administrations.

Terminal waveform fidelity assessment. After testing of the reference compounds (at 12 wk after surgery), rats were anesthetized by using thiobutabarbital (80 to 120 mg/kg IP, Inactin, Sigma-Aldrich Chemie GmbH, Buchs, Switzerland) and placed on a thermostatically controlled heating table to maintain body temperature at 36 to 38 °C. The trachea was intubated, and the lungs were ventilated (60 cycles/min, tidal volume: 6 to 9 mL; KTR5 small animal ventilator). A Millar high-fidelity catheter (2-French, model SPR-407, Millar Instruments) was inserted through the right ventricle into the pulmonary artery. A second Millar catheter was inserted in the right femoral artery and advanced into the abdominal aorta, near the tip of the channel-2 sensing catheter. An apex-to-base lead II electrocardiogram was recorded by biopotential electrodes. After equilibrium was established, pulmonary and systemic arterial blood pressure and electrocardiographic values were recorded for 30 min (PowerLab Data Acquisition System, IOX Data acquisition, EMKA Technologies). In parallel, tracings from the dual-pressure transmitter were continuously and simultaneously recorded by using Dataquest acquisition software (ART 4.3, Data Sciences International).

Organ sampling for histopathology. At the end of the waveform fidelity assessment, rats were euthanized by using intravenous pentobarbital (100 mg/kg, Esconarkon, Streuli Pharma, Uznach, Switzerland). Tissue samples were collected from the right ventricle, descending aorta, and pulmonary artery (from the sites of the pressure catheters); immersed and fixed in 4% buffered paraformaldehyde solution; and embedded in paraffin. Paraffin sections of the right ventricle, descending aorta, and pulmonary artery (2 µm thick) were deparaffinized, rehydrated, and stained with hematoxylin and eosin for histopathologic examination.

Statistical analysis. All data are presented as arithmetic mean ± SEM. Hourly data from each treatment group were pooled, and an unpaired Student t test was applied (Excel, Microsoft, Redmond, WA). Statistical significance was defined as a P value less than 0.05.

Results

Body weight. Body weight was monitored for 3 wk after implantation of the telemetry device. During the first 5 d after surgery, body weight decreased 6% to 12%; however, body weight gain returned to normal values by 1 wk after surgery. At 3 wk after implantation of the transmitter, body weight had increased 24% ± 1% (n = 8) compared with baseline values (P < 0.001, Figure 2).

Blood pressure and electrocardiographic variables. Between weeks 2 and 8 after surgery, a 24-h average of all hemodynamic variables was calculated weekly. Baseline values for MAP, MPAP, and heart rate were similar among all rats before administration of saline or monocrotaline at week 3 (Table 1). At week 7 (4 wk after injection), MPAP in saline-treated rats

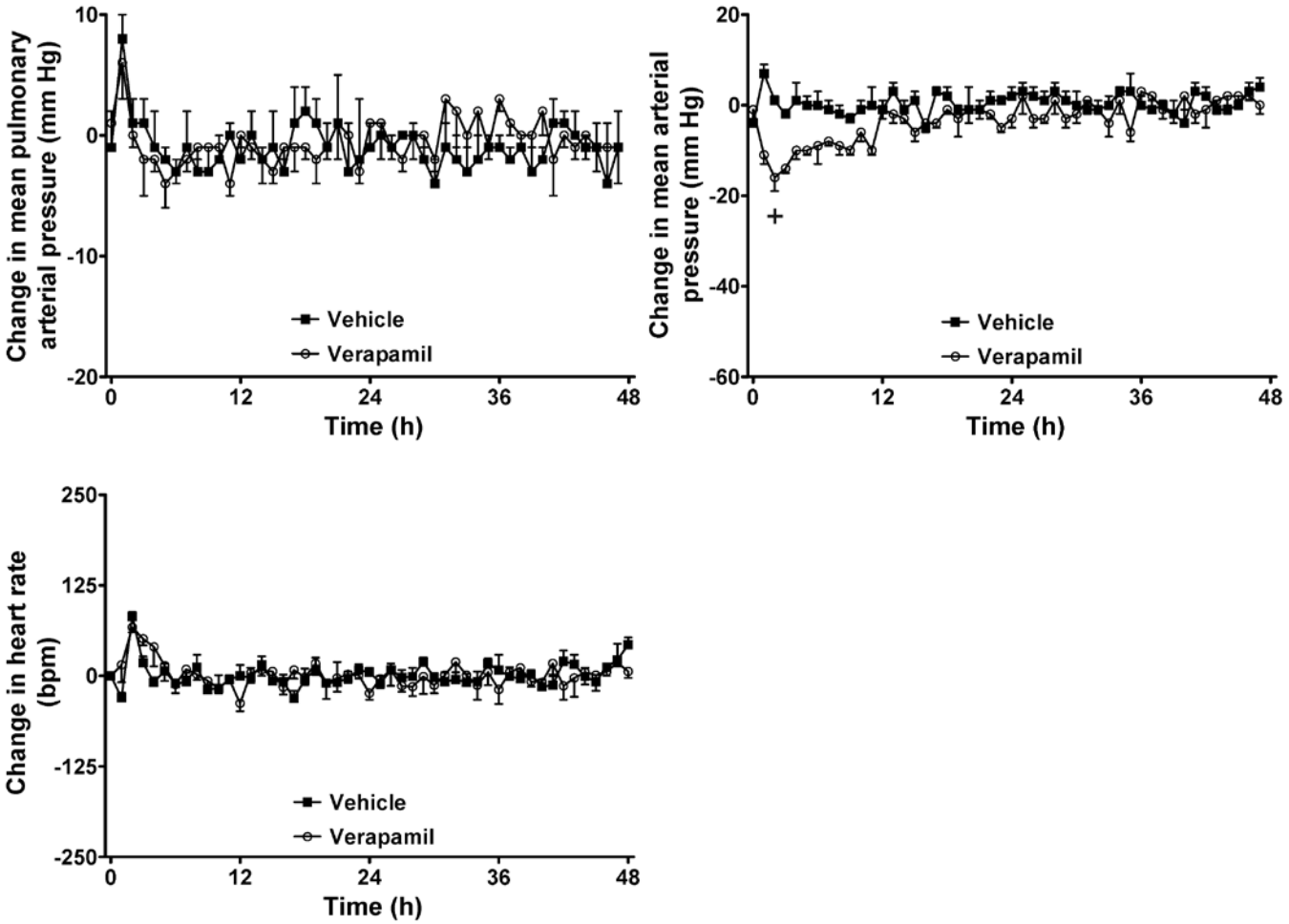

Figure 5. Effect of a single dose of verapamil (30 mg/kg PO) on mean pulmonary arterial pressure, mean arterial pressure, and heart rate in conscious, freely moving pulmonary hypertensive Wistar rats ($n = 4$). Data are presented as change in hourly mean ± SEM. +, Maximal decrease ($P < 0.01$) in mean arterial pressure was obtained 2 h after oral administration.

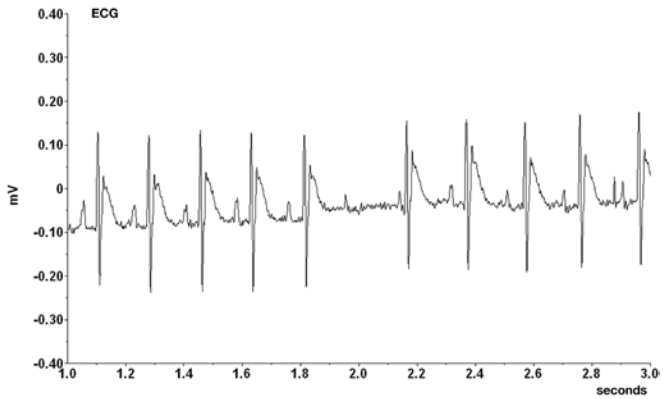

Figure 6. Representative electrocardiogram of a type II (Wenckebach) AV block after a single dose of verapamil (30 mg/kg PO) in a conscious, transmitter-implanted pulmonary hypertensive Wistar rat.

($n = 4$) decreased slightly (and nonsignificantly) by 9% (22 ± 1 to 20 ± 1 mm Hg) and MPAP in monocrotaline-treated rats ($n = 4$) increased by 77% (22 ± 0 to 39 ± 8 mm Hg); MAP values were unchanged. There were no differences in heart rate between the groups during the 8 wk after implantation of the telemetry system. The systemic arterial pulse pressure signal (systolic – diastolic arterial pressure) did not change over time in saline- (38 ± 1 to 37 ± 1 mm Hg) or monocrotaline-treated (37 ± 1 to 36 ± 2 mm Hg) rats. Compared with that at week 3, pulmonary arterial pulse pressure at week 7 (4 wk after injection) in monocrotaline-treated rats had increased by 183% (12.0 ± 0.4 to 33.9 ± 10.9 mm Hg) but had not changed in saline-treated rats (12.5 ± 0.4 to 12.7 ± 1.0 mm Hg).

Figure 3 A shows the systemic arterial pressure, pulmonary arterial pressure, and electrocardiographic intervals at 3 wk after surgery of a conscious, otherwise untreated Wistar rat implanted with a dual-pressure transmitter. Figure 3 B shows the same rat with pulmonary hypertension at 6 wk after exposure to monocrotaline (9 wk after surgery). Compared with baseline levels, systemic blood pressure remained unchanged whereas pulmonary artery blood pressure was increased enormously: systolic pulmonary artery blood pressure was as high as the systolic systemic arterial blood pressure. The electrocardiographic signal was clearly readable throughout the study. The novel dual blood-pressure transmitter was able to transmit blood pressure and electrocardiographic signals of very high quality throughout the entire 12-wk study.

Pharmacologic response to reference compounds. Administration of single dose of endothelin receptor antagonist (10 mg/kg PO) to normotensive rats did not affect MPAP, MAP, or heart rate compared with that in vehicle-treated rats (data not shown). However, a single dose endothelin receptor antagonist in monocrotaline-induced pulmonary hypertensive rats ($n = 4$) maximally decreased MPAP by 9 ± 2 mm Hg

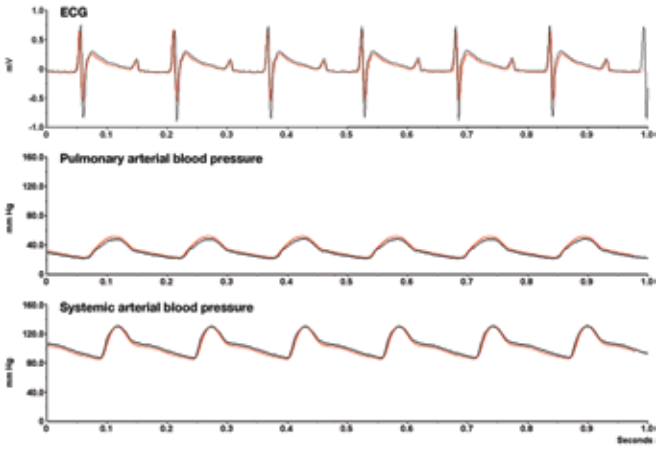

Figure 7. Simultaneous recording of the electrocardiogram, pulmonary arterial pressure, and systemic arterial pressure by using the dual blood-pressure telemetry transmitter (black lines) or 2 Millar high-fidelity blood pressure transducers (red lines).

($P = 0.096$), but MAP and heart rate remained similar to those in vehicle-treated animals (Figure 4). The maximal decrease in MPAP occurred 6 h after administration of endothelin receptor antagonist, and MPAP returned to baseline values after 24 h.

Administration of a single dose of verapamil (30 mg/kg PO) to monocrotaline-induced pulmonary hypertensive rats ($n = 4$) maximally decreased systemic MAP by 18 ± 2 mm Hg ($P < 0.01$) but did not affect MPAP or heart rate compared with those in vehicle-treated rats (Figure 5). The maximal decrease in MAP was obtained 2 h after verapamil administration and returned to baseline values after 12 h. Single-dose verapamil treatment of normotensive rats lowered the systemic blood pressure to a similar extent as that in pulmonary hypertensive rats and did not change MPAP or heart rate (data not shown). Analysis of the electrocardiographic tracings of verapamil-treated rats showed occasional second-degree (Wenckebach or Mobitz I) AV blocks (2 of 4 rats; Figure 6).[13] This category of second-degree AV blocks is characterized by progressive prolongation of the PR interval before failure of an atrial impulse to be conducted to the ventricles (a QRS complex is not generated).[14] After a Wenckebach AV block, the PR interval returns to baseline interval, and the sequence begins again.

After the reference compounds were tested, 2 Millar blood-pressure transducers (an invasive method) were used to collect systemic and pulmonary arterial blood pressures. The waveforms of the electrocardiogram, pulmonary arterial pressure, and systemic arterial pressure for the dual blood-pressure transmitter compared with the Millar transducers were very similar (Figure 7).

Local tissue tolerance. Histopathologic examination of the right ventricle (Figure 8 A) where the pulmonary artery transmitter catheter crossed the ventricular wall revealed granulomatous tissue (organized collection of macrophages and other inflammatory cells and collagen) in all rats. This alteration was a reaction to the injured myocardial tissue. The aorta at the placement site of the systemic blood pressure catheter was histologically normal (Figure 8 B). In 50% of rats, the placement site of the pulmonary catheter in the pulmonary artery presented with small foci of intimal thickening (Figure 8 C), which we considered to be due to the mechanical stress of the pulmonary catheter on the pulmonary trunk. Overall, the transmitter was very well tolerated.

Discussion

A newly designed, dual blood-pressure telemetry transmitter was implanted in the pulmonary artery and abdominal aorta in normotensive and monocrotaline-induced pulmonary hypertensive rats. Using this transmitter, we were able to simultaneously measure the pulmonary and systemic arterial blood pressures and electrocardiographic intervals in conscious, freely moving rats. The goal of the current study was to validate this new transmitter and not various pharmacologic compounds; we therefore kept the total number of rats used to a strict minimum for animal welfare reasons. Because of the high variability in induced pulmonary hypertension after monocrotaline treatment, our group sizes were insufficient to reach statistical significance.

As previously described,[7] a recovery period of 2 to 3 wk is necessary after thoracotomy and implantation of a telemetry device until hemodynamic variables are stable and animals return to normal body weight. Monocrotaline injection caused a progressive increase in pulmonary arterial pressure but did not affect systemic arterial pressure. With this treatment, systolic pulmonary arterial pressure increased more than diastolic pulmonary artery pressure (+ 100% compared with + 41%), as previously described.[7] The second part of the current study measured the hemodynamic effect of various cardiovascular reference compounds. Oral administration of an endothelin receptor antagonist to monocrotaline-induced pulmonary hypertensive rats lowered pulmonary arterial pressure to a similar extent as described in the literature, without affecting systemic arterial pressure and heart rate.[4] In contrast, oral administration of verapamil decreased systemic arterial pressure in normotensive rats as previously shown, [1] without affecting pulmonary arterial pressure or heart rate. The pulmonary arterial pressure, systemic arterial pressure, heart rate, and electrocardiographic values measured with the dual blood-pressure transmitter were very similar to single-pressure measurements recorded for rats implanted with a single pressure telemetry device (data not shown). Validation against 2 Millar high-fidelity blood pressure catheters at the end of the study confirmed the accuracy of the blood pressure data recorded with the novel transmitter. The signal waveform qualities of the transmitted variables (pulmonary arterial pressure, systemic arterial pressure, and electrocardiogram) were excellent throughout the entire 12-wk study. In addition, local tolerance of the associated catheters in target organs was confirmed by histologic examination.

This new telemetry device offers a more complete physiologic assessment from a single animal. It reduces the number of animals, associated costs (labor, compound, housing, and so forth), and interanimal variability associated with collecting a single pressure from 2 individual animals. The dual transmitter could be used for various small animal applications to measure, for example, left ventricular pressure and blood pressure, right ventricular pressure and blood pressure, pleural pressure and blood pressure, and bladder pressure and blood pressure. To avoid technical difficulties, the investigator should be experienced in microsurgical techniques.

In conclusion, the present study validates the use of a dual blood-pressure transmitter to simultaneously monitor 2 different arterial pressures, heart rate, and electrocardiographic variables. This technology represents a key advance in monitoring blood pressures and electrocardiographic measurements in a single, freely moving rat. In addition, use of the dual pressure telemetry device will reduce the number of animals required for experimentation. This device accommodates long-term monitoring and likely can be used in many chronic small animal models,

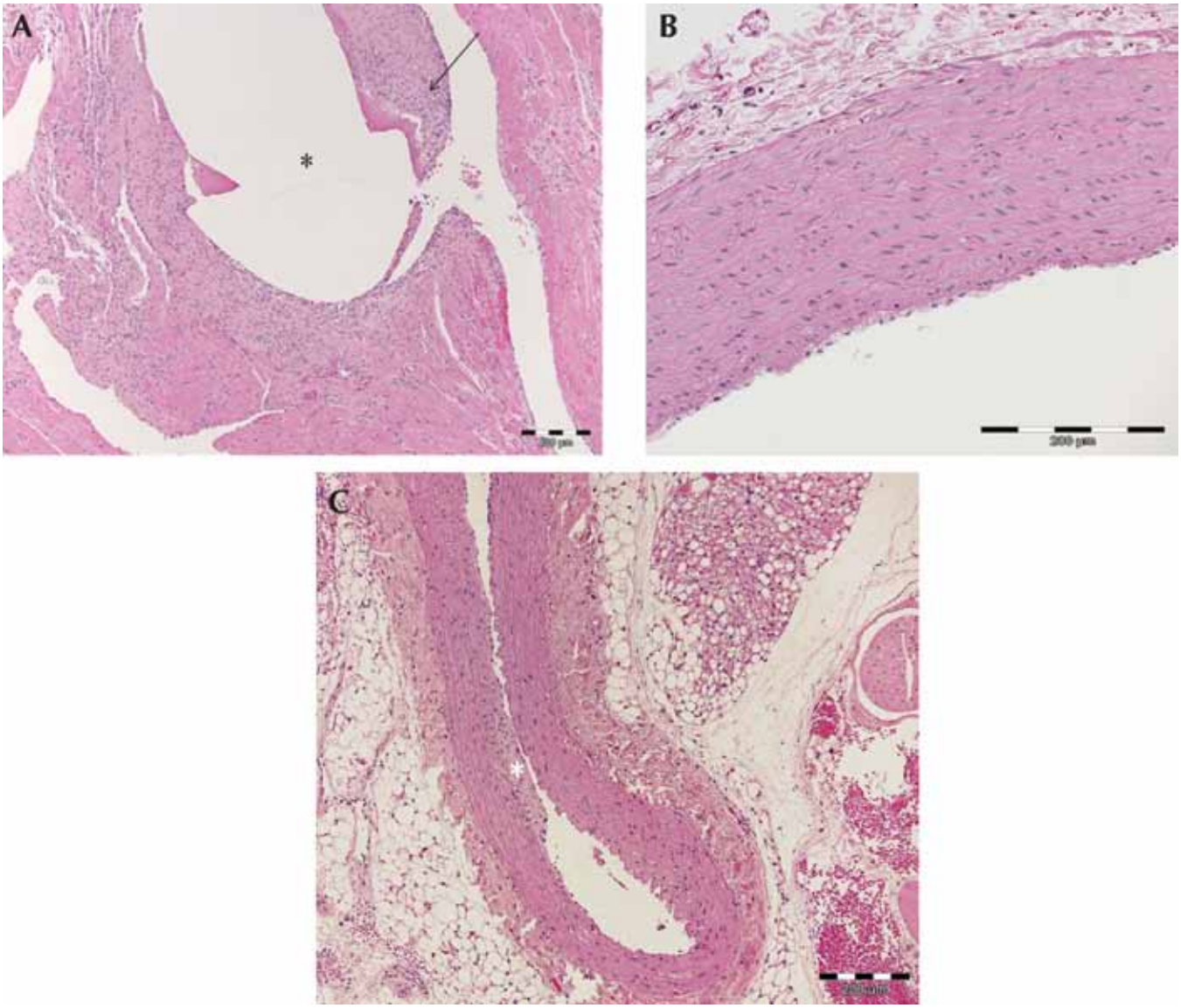

Figure 8. Histopathology of sites where the transmitter catheters were implanted. (A) Hematoxylin- and eosin-stained representative sample of granulomatous tissue (arrow) consisting of macrophages, other inflammatory cells, and fibrous components around the canal (*) of the right ventricular heart catheter. (B) No pathologic findings in the aorta. (C) Pulmonary artery with small focus of intimal thickening (*).

such as the monocrotaline-induced pulmonary hypertension rat model, to investigate the effects of new drugs.

Acknowledgments

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