Blood Pressure Characterization of Hypertensive and Control Rats for Cardiovascular Studies

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Introduction
Cardiovascular diseases are by far the most frequent causes of death in industrialized countries. An estimated 73 million American adults, nearly one in three, have high blood pressure (1). With this prevalence in cardiovascular disease, new tools to investigate these conditions can accelerate the process of finding solutions. Charles River’s disease models program supports these research efforts through providing available well characterized models of cardiovascular disease. Models available include: Spontaneous Hypertensive Rats (SHR), Wistar Kyoto Rat (WKY), Dahl salt-sensitive rats (DSS), and the Dahl/Salt Sensitive Rats (DSS). To insure that these models function as stated in the literature, a quality control process is necessary for characterizing and monitoring the blood pressure in these models. Described in this poster are the methods Charles River uses to monitor these models.

Material and Methods

Equipment
Databases (www.CRL końe) - A telemetry system manufactured by DATASCIENCE TECHNOLOGIES
BP-2000 Blood Pressure Analysis System
A tail-cuff pressure system manufactured by the Visitech System, Inc. ( Apex, NC, USA).

Animals and Husbandry
Four male and three female WKY rats at 8 weeks of age were instrumented with DSI telemetry devices (PA-C40). All animals were fed Charles River standard diet (Purina 5L79) ad libitum from weaning and throughout the study. Eight male and four female SHR rats at 8 weeks of age were surgically implanted with DSI telemetry devices. Additionally, four male and four female SHR rats were monitored using the BP-2000 tail-cuff system. All animals were fed Charles River standard diet (Purina 5L79) ad libitum from weaning and throughout the study. Eight male DDS rats at 8 weeks of age were surgically implanted with DSI telemetry devices. Four of these animals were implanted with the BP-2000 tail-cuff system. All animals were fed Charles River standard diet (Purina 5L79) ad libitum from weaning until 8 weeks of age. When they were placed on an AIN-76A with 8% salt diet (AIN-76A) for the remainder of the study period. All animals were singly housed in polycarbonate cages in a barrier procedure room that was kept at 21°C with a relative humidity of 40 - 60% and a 12-12 hour light-dark cycle.

Surgical Procedure

Tail-cuff Monitoring

The tail-cuff monitoring studies were performed using the BP-2000 tail-cuff system. All animals were singly housed in polycarbonate cages in a barrier procedure room that was kept at 21°C with a relative humidity of 40 - 60% and a 12-12 hour light-dark cycle. The animals were fed Charles River standard diet (Purina 5L79) ad libitum from weaning until 8 weeks of age. When they were placed on an AIN-76A with 8% salt diet (AIN-76A) for the remainder of the study period. All animals were singly housed in polycarbonate cages in a barrier procedure room that was kept at 21°C with a relative humidity of 40 - 60% and a 12-12 hour light-dark cycle.

Tail-cuff Monitoring

After the BP-2000 equipment was set up and configured, the selected animals were acclimated to the equipment once per day for two days before actual testing began. Animals were tested once per week for 10 weeks.

Results

WKY Direct Blood Pressure

As soon as the animals recovered from anesthesia, they were placed on the Dataquest system. During the first week post surgery, blood pressure decreased by about 10 mmHg for both male and female groups. When blood pressure in both groups became relatively stable during the study period, the average systolic, mean and diastolic pressure were 124, 101 and 82 mmHg respectively for the male rats. The average pressures for the female rats were 96, 81 and 66 mmHg respectively (Figures 1 & 2).

Discussion

WKY Rats: For both male and female groups, data collection was started immediately after animals recovered from anesthesia. The initial elevation of blood pressures was likely related to the postoperative recovery of the animals. The results of this study are in agreement with other literature reports (3, 4).

SHR Direct Blood Pressure

In the SHR male group, the systolic blood pressure consistently increased at a rate of 3.5 mmHg per week from 164 mmHg at 9 week of age to 185 mmHg at 15 week of age. The pressure then plateaued at an average of 187 mmHg during 16 to 28 weeks of age (Figure 3). In the SHR female group, the blood pressure remained fairly constant from 13 weeks of age through 28 weeks of age with an average of systolic pressure at 163 mmHg; mean pressure at 137 mmHg and diastolic pressure at 112 mmHg (Figure 4).

DSS Direct Blood Pressure

In the DSS rats fed the Charles River diet, the systolic blood pressure increased 14 mmHg during the study from 131 mmHg to 145 mmHg at 8 weeks of age. The mean average blood pressure and diastolic pressure was 108 and 89 mmHg respectively (Figure 6). In contrast, the systolic blood pressure of the animals fed 8% salt AIN76a diet steadily increased at an average rate of 14 mmHg per week at an average of 235 mmHg during the first 6 weeks on study. The mean blood pressures then decreased in the last two weeks of the study at a rate of 7 mmHg per week. The mean and diastolic pressures followed the same trend and the maximum values reached 199 and 172 mmHg respectively (Figure 8).

In the male group with direct telemetry technology, a gradual elevation of blood pressure with increasing age was observed. However, due to body size constraint of the female SHR rats and the need to use larger (older) animals, surgical implantation of telemetry device was not successful for female rats younger than 12 weeks of age. An increase in blood pressure over time was not observed.

The findings in this study are in agreement with other literature reports (3, 4). Although the increase in blood pressure with increasing age with blood pressure was observed in the indirect tail-cuff study group, the average of systolic pressure obtained by tail-cuff method was 12 mmHg higher than that measured with direct telemetry method during the 7 weeks of study. Tail-cuff technology is based on detecting tail blood flow or external tail pulse. A previous report documented a poor correlation between blood pressures recorded by tail-cuff technology and that measured by telemetry methodology (5). In contrast, this study demonstrates that results obtained by BP-2000 correlated well with findings of direct arterial catheter telemetry methods (6).

DSS Rats: The results of this study are in line with other literature reports (7, 8). Data from the high salt group indicates that animals develop hypertension during the first 6 weeks after being placed on the high salt diet. The decrease of blood pressure observed during the last 2 weeks suggests that those animals are experiencing heart failure. Clinical signs in these animals supported the blood pressure data trends.

Reference

2. Calhoun DA; Zhu ST; Chen YF; JH; HG; JU; JL; JU; LM; LU; MV; NL; NV; OW; ST; SL; SL; SM; SN; SP; U, WR; JT; ZA. Reduced Blood Pressure in Spontaneously Hypertensive Rats by TREAT. Hypertension. 2007;50: 801 -805.