Blood Pressure Characterization of Hypertensive and Control Rats for Cardiovascular Studies

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Y Luo, D Owens, G Mulder, A McVey, T Fisher   Charles River Laboratories, Wilmington, MA, USA

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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 prevelance in cardio-vascular disease, new tools to investigate these conditions can accelerate the process of finding solutions. Charles River's disease models program supports these research efforts by making available several rodent models of cardiovascular disease. Models available include: Spontaneous Hypertensive Rats (SHR), Wistar Kyoto Rats (WKY) - the SHR control strain, 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

Dataquest ART™ system - A telemetry system manufactured by DATA Sciences International (DSI - Minneapolis, MN, USA)
BP-2000 Blood Pressure Analysis System™ - A tail-cuff 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 labitum* 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. Furthermore, 4 male and 4 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 DSS rats at 8 weeks of age were surgically implanted with DSI telemetry devices. Four of these animals were fed Charles River standard diet (Purina 5L79) beginning at weaning and remained on the diet throughout the study. The other four rats were fed AIN-76A (Research Diets) diet containing 0.3% NaCl from weaning until 8 weeks of age when they were placed on an AIN-76A with 8% salt diet (8% 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 ±1°C with a relative humidity of 40 - 60% and a 12:12 hour light/dark cycle.

Surgical Procedure

Surgical implantation of the telemetry devices followed the IACUC approved protocol. Briefly, animals were anesthetized with Ketamine and Xylazine. An aseptic laparotomy was performed to expose the abdominal aorta. The catheter tip of the telemetry device was inserted into the aorta and secured with medical glue. The body of the telemetry device was left inside the abdominal cavity and secured to the abdominal wall during suture closure of the incision. Animals received post-operative analgesics (buprenorphine) and were allowed to recover from the anesthesia.

Telemetry Monitoring

After recovery from the anesthesia, rats were placed in individual cages and the cages placed on receivers. The Dataquest ART system was programmed to collect data on systolic, mean, and diastolic pressures at intervals of every 5 minutes for 10 second periods. The studies were run for 8 to 20 weeks depending on the model and purpose of measurements.

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 121 (systolic), 99 (mean) and 80 (diastolic) mmHg (Figures 1 & 2).

Figure 1: Blood Pressure, Direct, Male WKY Rats on Purina 5L79 Diet

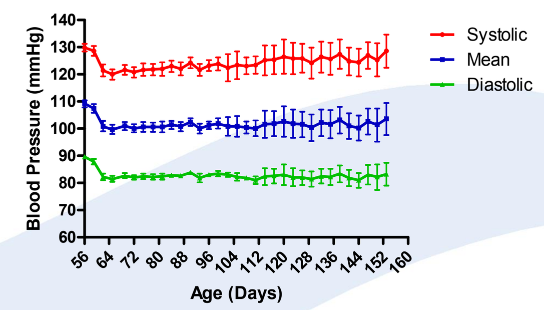
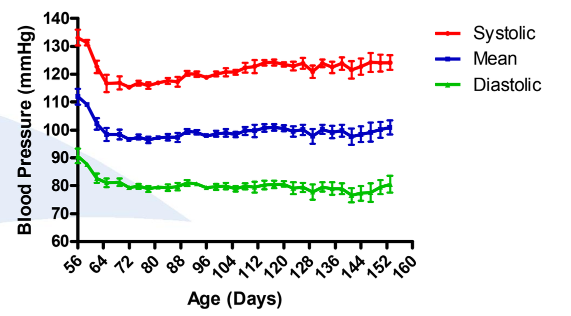


Figure 2: Blood Pressure, Direct, Female WKY Rats on Purina 5L79 Diet



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 average of systolic pressure at 163 mmHg; mean pressure at 137 mmHg and diastolic pressure at 112 mmHg (Figure 4).

Figure 3: Blood Pressure, Direct, Male SHR on Purina 5L79 Diet

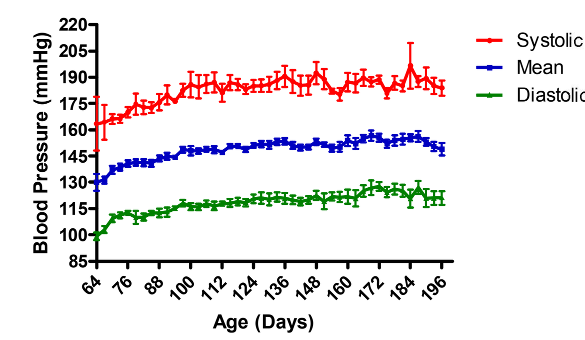
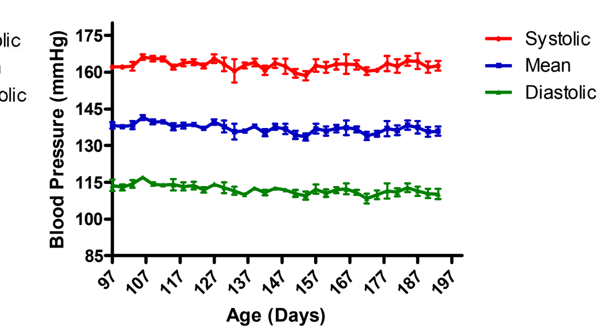


Figure 4: Blood Pressure, Direct, Female SHR on Purina 5L79 Diet



SHR Indirect Blood Pressure

In the SHR male group, the systolic blood pressure consistently increased at an average rate of 4.43 mmHg per week from 172 mmHg at 8 weeks of age to 203 mmHg at 15 weeks of age (Figure 5). The mean and diastolic pressures increased from 139 and 125 mmHg to 186 and 176 mmHg respectively within 7 weeks. In the SHR female group, the blood pressure increased weekly from 154 (systolic), 119 (mean) and 100 (diastolic) mmHg at 8 weeks of age to 191, 166 and 154 mmHg respectively at 15 weeks of age (Figure 6).

Figure 5: Blood Pressure, Indirect, Male SHR on Purina 5L79 Diet

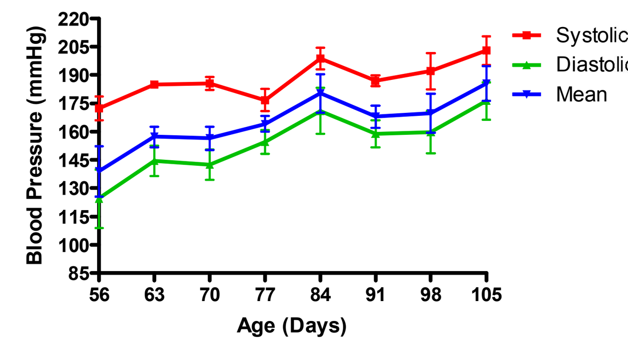
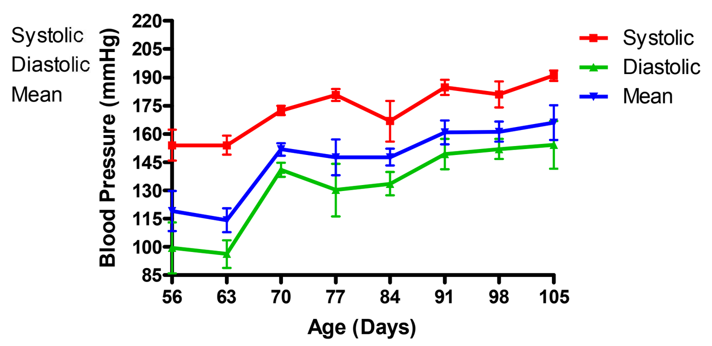


Figure 6: Blood Pressure, Indirect, Female SHR on Purina 5L79 Diet



DSS Direct Blood Pressure

In the DSS rats fed the Charles River diet, the systolic blood pressure increased 14 mmHg during the 7 week study with an average of 131 mmHg. The average mean blood pressure and diastolic pressure was 108 and 89 mmHg respectively (Figure. 7). In contrast, the systolic blood pressure of the animals fed 8% salt AIN76a diet steadily increased at an average rate of 14.3 mmHg per week to as high as 230 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).

Figure 7: Blood Pressure, Direct, Male Dahl/SS Rats on Purina 5L79 Diet

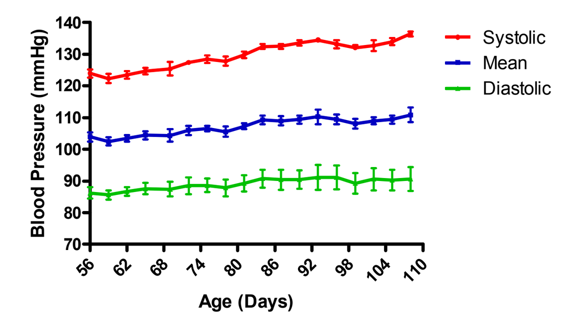
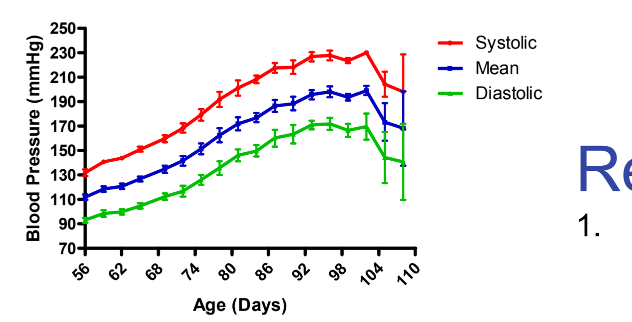


Figure 8: Blood Pressure, Male Dahl/SS Rats on 8% Salt AIN76a Diet



Discussion

<u>WKY Rats</u>: 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 reports in literature (2,4,7).

<u>SHR Rats</u>: 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 same trends of blood pressure increasing with age were observed in the indirect tail-cuff study groups, 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, others found that results obtained by BP-2000 correlated well with findings of direct arterial catheter and transducer methods (6).

<u>DSS Rats</u>: 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 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

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