Overlap Between Whites and Blacks in Response to Antihypertensive Drugs

Ashwini R. Sehgal

Abstract—On average, whites and blacks differ in their response to specific antihypertensive drugs. These differences are often highlighted in reviews and practice guidelines. However, there is wide variation in drug-associated changes in blood pressure within each race. The goal of this meta-analysis is to quantitate how often whites and blacks have similar responses to specific antihypertensive drugs. Computerized searches of MEDLINE (1983 to March 2003) and manual searches of references listed in identified articles were performed. Studies were included if they provided race-specific changes in blood pressure. Fifteen studies with a total of 9307 white subjects and 2902 black subjects were analyzed. For drug-associated changes in diastolic blood pressure, the mean difference between whites and blacks ranged from 0.6 to 3.0 mm Hg while the standard deviation within each race ranged from 5.0 to 10.1 mm Hg. The percentage of whites and blacks with similar drug-associated changes in diastolic blood pressure ranged from 83% to 93%. In conclusion, the majority of whites and blacks have similar responses to commonly used antihypertensive drugs. Clinical decisions to use a specific drug should be based on other considerations such as efficacy in individual patients, compelling indications, and cost. (Hypertension. 2004;43:566-572.)

Key Words: hypertension ■ drug therapy ■ race ■ meta-analysis

On average, whites and blacks differ in their response to many antihypertensive drugs. For example, a large multicenter study found that administration of the angiotensin-converting enzyme inhibitor captopril led to a 10.7 mm Hg reduction in diastolic blood pressure among whites and an 8.0 mm Hg reduction among blacks, resulting in a white–black difference of 2.7 mm Hg (P<0.001).1 In general, whites appear to respond better to β-blockers and angiotensin-converting enzyme inhibitors whereas blacks appear to respond better to diuretics and calcium channel blockers.2 These average differences are often highlighted in reviews and practice guidelines.2–5 However, there is wide variation in drug-associated changes in blood pressure within each race. In the captopril study mentioned, the standard deviation within each race was 8 to 9 mm Hg, or more than 3-times larger than the white–black difference.1 This variation may mean that many whites and blacks have similar responses to specific drugs (Figure 1). Quantitating the extent of overlap between whites and blacks may guide clinicians as they select antihypertensive drugs for individual patients. The goal of this meta-analysis is to quantify the extent of overlap among all clinical trials in the past 20 years that report race-specific changes in blood pressure for commonly used antihypertensive drugs (ie, among the top 200 most prescribed drugs).6

Methods

Selection of Clinical Trials

Studies were identified through computerized bibliographic searches of MEDLINE (1983 to March 2003) supplemented with manual search of references listed in identified articles. The indexing terms were hypertension (major topic), clinical trial (publication type), human (study group), adult (ages), English (language), and black(s), race, racial, or African-American(s) (text words). Studies were included if they provided race-specific changes in blood pressure (mean and SD) for individual antihypertensive drugs. Studies were excluded if they involved concurrent administration of 2 or more drugs or other interventions (eg, dietary salt modification), used uncommon or experimental drugs, focused exclusively on patients with abnormal cardiac or renal function, or did not include whites and blacks. From the 428 articles identified, 15 studies met all selection criteria. Of the remaining 413 articles, 195 did not include concurrent administration of 2 or more drugs or other interventions, 14 focused on patients with abnormal renal or cardiac function, 18 included concurrent interventions, 26 used uncommon or experimental drugs, 5 duplicated other articles, 102 did not include whites and blacks, and 53 did not provide race-specific changes in blood pressure.

Data Extraction

Study characteristics included drug name and daily dose, treatment duration, and number of white and black subjects. Study findings included race-specific changes in systolic and diastolic blood pres-
sure (mean and SD) after drug treatment. Placebo responses were not included in this meta-analysis.

Statistical Analysis

Study findings were pooled separately for each drug category (diuretic, β-blocker, calcium channel blocker, angiotensin-converting enzyme inhibitor, α-blocker, central α-agonist). Specifically, the mean decrement in systolic blood pressure among white subjects in each study was weighted by the inverse of the variance. These weighted mean differences were then pooled across all studies.7,8 Similar calculations were performed to pool decrements in diastolic blood pressure among whites, decrements in systolic and diastolic blood pressure among blacks, and standard deviations associated with decrements in blood pressure. For studies within each drug category, the Q statistic showed no evidence of heterogeneity while funnel plots showed no evidence of publication bias (not shown).7,8

The pooled results were used to determine how often whites and blacks have similar responses to specific antihypertensive drugs. Because previous studies indicate that changes in blood pressure are normally distributed, the following 5 steps were performed.9,10 First, the pooled mean difference and SDs were used to mathematically describe the normal distributions corresponding to each race (Figure 1). Second, the intersection point of the 2 normal distributions was determined. Third, the area under the leftmost curve to the right of the intersection point was determined. Fourth, the area under the rightmost curve to the left of the intersection point was determined. Fifth, the 2 areas were added and expressed as a percentage of the total area under each curve. A similar procedure was used if the curves intersected at more than one point.

Results

Study Characteristics

The 15 trials analyzed involved a total of 9307 white subjects and 2902 black subjects with a treatment duration that ranged from 4 to 18 weeks (Table 1). All studies were hypertension trials (as opposed to other clinical trials that simply included antihypertensive agents). Most studies were randomized controlled trials and involved blinded administration of antihypertensive drugs. Among trials that reported mean baseline blood pressure separately for each race, blacks generally had a baseline diastolic blood pressure that was 2 to 4 mm Hg higher than whites.

Study Findings

A statistically significant difference between whites and blacks was found in several of the studies (Table 2). For example, study 1 found that whites had a 14.7 mm Hg decrement in systolic blood pressure after captopril administration whereas blacks had a 9.1 mm Hg decrement, a white–black difference of 5.6 (95% CI: 2.4 to 8.8). In all studies, the magnitude of the white–black difference was smaller than the SD within each race. For example, study 1 found that the SD within each race was approximately 15 mm Hg for change in systolic blood pressure. In addition,
TABLE 2. Findings of Clinical Trials of Antihypertensive Drugs

<table>
<thead>
<tr>
<th>Trial</th>
<th>Drug &amp; Dose (mg/d)</th>
<th>Systolic White Mean</th>
<th>Systolic Black Mean</th>
<th>Systolic White–Black Difference</th>
<th>Diastolic White Mean</th>
<th>Diastolic Black Mean</th>
<th>Diastolic White–Black Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Captopril 37.5–150</td>
<td>14.7</td>
<td>9.1</td>
<td>5.6</td>
<td>14.8</td>
<td>15.3</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Propranolol 80–480</td>
<td>9.5</td>
<td>1.4</td>
<td>10.9</td>
<td>11.8</td>
<td>11.8</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Enalapril 5–40</td>
<td>19.2</td>
<td>8.2</td>
<td>11.0</td>
<td>19.7</td>
<td>18.7</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Diltiazem 120–360</td>
<td>15.4</td>
<td>10.8</td>
<td>4.6</td>
<td>17.9</td>
<td>13.6</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Lisinopril 160–480</td>
<td>14.6</td>
<td>8.5</td>
<td>6.1</td>
<td>16.3</td>
<td>15.5</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Captopril 50–150</td>
<td>10.9</td>
<td>11.2</td>
<td>−0.3</td>
<td>9.5</td>
<td>17.4</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Nifedipine 30–120</td>
<td>16.5</td>
<td>15.0</td>
<td>−1.5</td>
<td>16.7</td>
<td>19.4</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Atenolol 50–100</td>
<td>9.1</td>
<td>4.6</td>
<td>−4.5</td>
<td>15.1</td>
<td>16.9</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Lisinopril 10–40</td>
<td>8.3</td>
<td>9.1</td>
<td>−0.8</td>
<td>10.4</td>
<td>9.4</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Nifedipine 30–120</td>
<td>13.2</td>
<td>15.3</td>
<td>−2.1</td>
<td>16.7</td>
<td>19.4</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Atenolol 25–100</td>
<td>14.0</td>
<td>7.0</td>
<td>7.0</td>
<td>11.0</td>
<td>11.0</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Captopril 11.0</td>
<td>11.0</td>
<td>8.0</td>
<td>3.0</td>
<td>9.0</td>
<td>11.0</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Clonidine 0.2–0.6</td>
<td>16.0</td>
<td>13.0</td>
<td>3.0</td>
<td>12.0</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Diltiazem 120–360</td>
<td>11.0</td>
<td>14.0</td>
<td>−3.0</td>
<td>9.0</td>
<td>10.0</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>HCTZ 12.5–50</td>
<td>12.0</td>
<td>14.0</td>
<td>−2.0</td>
<td>11.0</td>
<td>9.0</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Prazosin 4–20</td>
<td>8.0</td>
<td>8.0</td>
<td>0.0</td>
<td>9.0</td>
<td>12.0</td>
<td></td>
</tr>
</tbody>
</table>

(continues)
the direction of the race difference was not always consistent across studies. For example, whites had a larger response than blacks to diltiazem in study 4 whereas blacks had a larger response in study 5.

**Pooled Decrement in Blood Pressure After Drug Treatment**

On average, ß-blockers and angiotensin-converting enzyme inhibitors resulted in larger decrements among whites compared with blacks (indicated by positive white–black difference in Table 3). By contrast, diuretics and calcium channel blockers resulted in larger decrements among blacks (negative white–black difference). However, the white–black differences were small compared with the variation within each race. For example, the white–black difference in systolic blood pressure with angiotensin-converting enzyme inhibitors was 4.6 mm Hg whereas the SD within each race was approximately 12 to 14 mm Hg. In addition, the magnitude of the variation among whites was generally similar to the magnitude of the variation among blacks. For example, the SD for change in systolic blood pressure with diuretics was approximately 12 to 14 mm Hg. In addition, the magnitude of the variation among whites was generally similar to the magnitude of the variation among blacks. For example, the SD within each race was

**Overlap Among Blacks and Whites**

The majority of whites and blacks had similar responses to all categories of antihypertensive drugs (Figure 2). For example, 90% (95% CI: 83 to 97) of whites and blacks had similar changes in diastolic blood pressure with ß-blockers.

**Achieving Blood Pressure Goal**

The pooled means and SDs in Table 3 may be used to estimate the proportion of subjects achieving a specified decrement in blood pressure. These estimates are presented in Table 4 for ß-blockers and illustrate the impact of baseline blood pressure in determining the proportion of patients reaching a target blood pressure. For example, if whites and blacks are both 6 mm Hg above a target diastolic blood pressure at baseline, then use of this antihypertensive drug will help 77% of whites and 68% of blacks to achieve the target, resulting in a white–black difference of 8% (95% CI: 1 to 15). However, if blacks are 8 mm Hg above the target blood pressure at baseline (while whites are still 6 mm Hg above the target), then drug use will help 77% of whites and 58% of blacks to achieve the target, resulting in a larger white–black difference of 19% (95% CI: 12 to 26). If blacks are 10 mm Hg above the target at baseline, then 77% of whites and 47% of blacks will achieve the target, resulting in an even larger white–black difference of 30% (95% CI: 23 to 37).

**Discussion**

These results confirm the existence of modest average differences between whites and blacks in response to antihypertensive drugs. Whites generally responded better to ß-blockers and angiotensin-converting enzyme inhibitors whereas blacks generally responded better to diuretics and calcium channel blockers. More importantly, this meta-analysis of 15 clinical trials shows that approximately 80% to 95% of whites and blacks have similar responses to commonly used antihypertensive drugs (ie, even more overlap than that illustrated in Figure 1). The generalizability of these findings is enhanced by the comprehensive literature review, the large sample size of 12 209 patients, and the similarity of results across all drug categories.

It may be argued that achieving a treatment goal (eg, diastolic blood pressure <90 mm Hg) is more clinically relevant than the magnitude of blood pressure reduction. In fact, many previous studies have noted large discrepancies in the proportion of whites and blacks achieving a target blood pressure. For example, 90% of white subjects in one study achieved the treatment goal with an angiotensin-converting enzyme inhibitor whereas only 65% of black subjects did so, resulting in a racial difference of 25%.11 However, black
subjects in this study had baseline diastolic blood pressures that were 4 mm Hg higher than white subjects. This meta-analysis found that similarly small differences in baseline blood pressure are critical determinants of the likelihood of achieving a treatment goal (Table 3). For example, there was an 8% racial difference with beta-blocker use if whites and blacks were both 6 mm Hg above a treatment goal at baseline. This difference increased to 30% if blacks were 10 mm Hg above a treatment goal at baseline (while blacks were still 6 mm Hg above goal). Most previous studies that reported race-specific baseline blood pressures (Table 1) had a 2- to 4-mm Hg higher baseline diastolic blood pressure among blacks compared with whites. Thus, these studies may overestimate the difference in the proportion of whites and blacks achieving a target blood pressure after administration of a specific antihypertensive drug. Many other studies did not report baseline blood pressure separately for whites and blacks (Table 1), thereby making it difficult to interpret their results regarding racial differences in achieving a treatment goal.

These findings are relevant to recent debate about the role of racial, genetic, and environmental factors in explaining variation across individuals in drug response. Two key questions in this debate are (1) what are the most important genetic and environmental determinants of drug response and (2) is race a good proxy for such genetic and environmental determinants? If race is a good proxy for relevant genetic and/or environmental determinants of drug response, then clinicians should consider race in selecting drugs for individual patients. However, this meta-analysis found that race has little value in predicting antihypertensive drug response, because whites and blacks overlap greatly in their response to

### Table 3. Pooled Estimates of Decrement in Blood Pressure With Antihypertensive Drug Treatment

<table>
<thead>
<tr>
<th>Drug Category</th>
<th>White Mean</th>
<th>Black Mean</th>
<th>White–Black Difference</th>
<th>White SD</th>
<th>Black SD</th>
<th>White Mean</th>
<th>Black Mean</th>
<th>White–Black Difference</th>
<th>White SD</th>
<th>Black SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretic</td>
<td>11.5</td>
<td>15.0</td>
<td>-3.5</td>
<td>11.2</td>
<td>9.8</td>
<td>9.1</td>
<td>10.7</td>
<td>-1.5</td>
<td>6.2</td>
<td>6.2</td>
</tr>
<tr>
<td></td>
<td>(9.5, 13.4)</td>
<td>(13.1, 17.0)</td>
<td>(-6.4, -0.5)</td>
<td>(9.2, 13.2)</td>
<td>(7.8, 11.7)</td>
<td>(8.1, 10.1)</td>
<td>(9.5, 11.9)</td>
<td>(-3.1, 0.1)</td>
<td>(5.3, 7.2)</td>
<td>(5.0, 7.4)</td>
</tr>
<tr>
<td>B-blocker</td>
<td>11.7</td>
<td>5.9</td>
<td>6.0</td>
<td>14.2</td>
<td>13.0</td>
<td>11.3</td>
<td>9.5</td>
<td>2.9</td>
<td>7.2</td>
<td>7.3</td>
</tr>
<tr>
<td></td>
<td>(10.2, 13.3)</td>
<td>(4.2, 7.6)</td>
<td>(3.6, 8.3)</td>
<td>(12.7, 15.8)</td>
<td>(11.3, 14.6)</td>
<td>(10.5, 12.1)</td>
<td>(8.5, 10.4)</td>
<td>(1.6, 4.2)</td>
<td>(6.4, 8.0)</td>
<td>(6.3, 8.3)</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>15.3</td>
<td>16.9</td>
<td>-2.4</td>
<td>12.7</td>
<td>11.3</td>
<td>12.6</td>
<td>13.3</td>
<td>-0.6</td>
<td>6.5</td>
<td>6.3</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>12.8</td>
<td>8.5</td>
<td>4.6</td>
<td>12.3</td>
<td>13.9</td>
<td>11.4</td>
<td>8.0</td>
<td>3.0</td>
<td>6.9</td>
<td>8.4</td>
</tr>
<tr>
<td></td>
<td>(11.7, 13.9)</td>
<td>(7.0, 9.9)</td>
<td>(2.7, 6.5)</td>
<td>(11.2, 13.4)</td>
<td>(12.4, 15.3)</td>
<td>(10.8, 12.0)</td>
<td>(7.1, 8.9)</td>
<td>(1.9, 4.1)</td>
<td>(6.3, 7.5)</td>
<td>(7.5, 9.2)</td>
</tr>
<tr>
<td>a-blocker</td>
<td>18.0</td>
<td>16.5</td>
<td>1.5</td>
<td>15.5</td>
<td>19.8</td>
<td>13.2</td>
<td>12.7</td>
<td>0.5</td>
<td>7.8</td>
<td>10.1</td>
</tr>
<tr>
<td></td>
<td>(17.6, 18.4)</td>
<td>(15.4, 17.5)</td>
<td>(-0.3, 1.6)</td>
<td>(15.2, 15.9)</td>
<td>(18.7, 20.8)</td>
<td>(13.0, 13.4)</td>
<td>(12.2, 13.3)</td>
<td>(-0.3, 0.7)</td>
<td>(7.6, 7.9)</td>
<td>(9.5, 10.6)</td>
</tr>
<tr>
<td>Central a-agonist</td>
<td>16.6</td>
<td>14.4</td>
<td>2.4</td>
<td>12.6</td>
<td>11.7</td>
<td>13.7</td>
<td>11.1</td>
<td>2.6</td>
<td>5.0</td>
<td>7.0</td>
</tr>
<tr>
<td></td>
<td>(14.0, 19.2)</td>
<td>(11.8, 16.9)</td>
<td>(-2.1, 5.3)</td>
<td>(10.0, 15.2)</td>
<td>(9.1, 14.2)</td>
<td>(12.6, 14.7)</td>
<td>(9.6, 12.6)</td>
<td>(0.6, 4.2)</td>
<td>(4.0, 6.0)</td>
<td>(5.5, 8.5)</td>
</tr>
</tbody>
</table>

SD indicates standard deviation; ACE, angiotensin-converting enzyme. Values in parentheses represent 95% confidence intervals.

![Figure 2. Percent overlap between whites and blacks in response to antihypertensive drugs. Bars represent 95% confidence intervals.](image-url)
In conclusion, whites and blacks generally respond similarly to all major categories of antihypertensive drugs. This study’s method of measuring overlap may be helpful in assessing other types of health disparities. Clinicians and researchers should evaluate average differences and overlap between groups when examining health disparities.

Acknowledgments
Supported by grant DK51472 from the National Institute of Diabetes and Digestive and Kidney Diseases.

References
Overlap Between Whites and Blacks in Response to Antihypertensive Drugs
Ashwini R. Sehgal

Hypertension. 2004;43:566-572; originally published online February 2, 2004;
doi: 10.1161/01.HYP.0000118019.28487.9c

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2004 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/43/3/566

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org/subscriptions/