The Cerebral Hemodynamic Response to Administration of Hydralazine

By GEORGE G. ROWE, M.D., GEORGE M. MAXWELL, M.D., AND CHARLES W. CRUMPTON, M.D.

P RECEDING INVESTIGATIONS have shown that administration of hydralazine (1-hydrazinophthalazine) is accompanied by an increase in cardiac output,1-5 particularly if the decrease in blood pressure subsequent to its administration is not excessive,5 and by increased renal,6 hepatic,4 and coronary7 blood flow. Cerebral blood flow has been reported to be unchanged by hydralazine, even though cerebral vascular resistance decreased significantly after its administration.8

Material and Methods

This study was performed on five hypertensive subjects (three Smithwick grade IV, one grade III, and one grade II), and one subject who had labile blood pressure but was not hypertensive at the time of the study. All subjects were fasting. The drug was administered intravenously as a single dose to all subjects except the one with labile blood pressure in whom a supplemental intravenous dose was given. The dose of hydralazine ranged from 0.2 mg./Kg. to 0.3 mg./Kg., and the average dose was 0.25 mg./Kg. The interval between administration of the drug and the second determination of cerebral blood flow varied from 32 to 42 minutes, with an average of 37 minutes for five of the subjects. In the other subject, 0.24 mg./Kg. of hydralazine was given 52 minutes before the second study and 0.08 mg./Kg. 33 minutes before the second study because the change in blood pressure was not significant subsequent to the first dose.

Cerebral blood flow was determined by the nitrous oxide saturation method of Kety and Schmidt.9 Internal jugular bulb blood was obtained through a percutaneously placed needle. A Cour- nand needle was placed in a peripheral artery and attached by plastic tubing to a heparin-filled manifold for rapid sampling. Pressures were measured either directly by a mercury manometer or by a Statham strain-gage recording on the Sanborn Poly-viso with the mean determined by electrical integration. Arterial and cerebral venous blood specimens were analyzed for oxygen and carbon dioxide content by the Van Slyke-Neill manometric technic. Vascular resistance is expressed in units obtained by dividing mean arterial blood pressure by cerebral flow in milliliters per 100 Gm. of brain tissue per minute.

Results

The results of this study are summarized in table 1. The heart rate increased 20.5 per cent (p < 0.05) subsequent to administration of hydralazine, whereas the mean arterial blood pressure decreased by 17.5 per cent (p < 0.05). Following the administration of the drug, the arterial oxygen content increased by 2.9 per cent (p < 0.01), whereas the internal jugular oxygen content increased by 24.8 per cent (p < 0.01) with a 25.7 per cent decrease in the arteriovenous oxygen difference (p < 0.01). The arterial carbon dioxide content decreased by 7.7 per cent (p < 0.01), whereas the internal jugular carbon dioxide content decreased by 8.9 per cent (p < 0.01) and the internal jugular-arterial carbon dioxide difference, although less, was sufficiently variable that it did not decrease significantly. The cerebral respiratory quotient increased slightly but not significantly. Cerebral blood flow increased by 31.8 per cent (p < 0.05), whereas cerebral vascular resistance decreased by 34.8 per cent (p < 0.05) and cerebral oxygen consumption and carbon dioxide production remained unchanged.

Discussion

There is reason to believe from preceding studies of hydralazine that its hemodynamic
Table 1

<table>
<thead>
<tr>
<th></th>
<th>Before ± SEM*</th>
<th>After ± SEM*</th>
<th>% Change</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>88 ± 3.4</td>
<td>106 ± 6.4</td>
<td>+20.5</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Mean arterial blood pressure (mm, Hg)</td>
<td>143 ± 12.8</td>
<td>118 ± 8.5</td>
<td>-17.5</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Arterial oxygen content†</td>
<td>17.5 ± 0.8</td>
<td>18.0 ± 0.9</td>
<td>+ 2.9</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Internal jugular oxygen content†</td>
<td>10.1 ± 0.8</td>
<td>12.6 ± 1.2</td>
<td>+24.8</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Arterial-internal jugular oxygen difference†</td>
<td>7.4 ± 0.2</td>
<td>5.5 ± 0.5</td>
<td>-25.7</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Internal jugular carbon dioxide content†</td>
<td>54.2 ± 2.7</td>
<td>49.4 ± 3.1</td>
<td>-8.9</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Arterial carbon dioxide content†</td>
<td>48.0 ± 2.6</td>
<td>44.3 ± 2.7</td>
<td>-7.7</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Internal jugular-arterial CO₂ difference†</td>
<td>6.3 ± 0.4</td>
<td>5.1 ± 0.6</td>
<td>-19.1</td>
<td>&lt; 0.2</td>
</tr>
<tr>
<td>Cerebral respiratory quotient</td>
<td>0.85 ± 0.06</td>
<td>0.93 ± 0.03</td>
<td>+ 9.4</td>
<td>&lt; 0.3</td>
</tr>
<tr>
<td>Cerebral blood flow‡</td>
<td>44 ± 4.1</td>
<td>58 ± 7.4</td>
<td>+31.8</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Cerebral vascular resistance</td>
<td>3.31 ± 0.31</td>
<td>2.16 ± 0.25</td>
<td>-34.8</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>(Units: MARP ÷ CBF)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral oxygen consumption‡</td>
<td>3.3 ± 0.3</td>
<td>3.2 ± 0.5</td>
<td>-3.0</td>
<td>&gt; 0.9</td>
</tr>
<tr>
<td>Cerebral carbon dioxide release‡</td>
<td>2.8 ± 0.3</td>
<td>3.0 ± 0.4</td>
<td>+ 7.2</td>
<td>&lt; 0.8</td>
</tr>
</tbody>
</table>

*SEM = Standard error of the mean.
†mL/100 ml. of blood.
‡mL/100 Gm./minute.

Effect differs from ganglion-blocking drugs, since it reduces peripheral vascular resistance and increases cardiac output as well as hepatic, renal, and coronary blood flow. This study reveals that the decrease in vascular resistance demonstrable in other vascular systems occurs also in the cerebral vascular bed as manifested by an increase in cerebral flow while the arterial blood pressure is reduced. The discrepancy between the present study, in which cerebral blood flow increased, and the preceding report, in which cerebral vascular resistance decreased but blood flow was unchanged, is possibly due to differences in dose, in route of administration (intravenous versus intramuscular), or to the longer interval between the administration of the drug and the study in the former report. The time interval may well be a very important factor in this discrepancy, since the preceding study was done when the blood pressure was stable at its lowest level or had begun to rise and the hyperemia may well be transient, so that a study done at this time might reveal a different result. It is also apparent that the cerebral blood flow in the present group was lower and the cerebral vascular resistance higher before hydralazine administration than in the preceding study. Furthermore, in the present group, hydralazine increased cerebral blood flow in spite of a decrease in the arterial and internal jugular blood carbon dioxide contents. This seems particularly significant in view of the known reduction in cerebral blood flow that occurs with hyperventilation and hypocapnia. Arterial and mixed venous blood carbon dioxide content decreased in preceding studies of this drug as well, and presumably may be attributed to the increase in the minute volume of ventilation that occurs after administration of hydralazine. Cardiac output was measured in two of these subjects during the same study as cerebral blood flow was determined and was shown to increase considerably (+47 per cent and +63 per cent). Since there was no major decrease in blood pressure of any of the subjects, and since previous studies have shown that cardiac output tends to rise unless the blood pressure fall is great, it may be presumed that cardiac output increased in the other subjects as well and that the increased cerebral blood flow is a localized manifestation of generalized hyperemia. The present data bring the response of the cerebral vascular bed to hydralazine into line with
changes reported previously in studies of other regional vascular beds,4.6,7 presenting a more uniform picture of its hemodynamic action.

Conclusions
Cerebral blood flow has been studied in a series of five hypertensive subjects and one normotensive subject before and after administration of hydralazine.

Subsequent to intravenous administration of hydralazine (average dose = 0.25 mg./Kg.) there was a simultaneous increase in pulse rate and decrease in blood pressure, whereas cerebral vascular resistance decreased and cerebral blood flow increased.

The arteriovenous oxygen difference across the brain narrowed, and cerebral oxygen consumption was maintained unchanged.

References
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