The Effect of Amytal on the Cardiac Output and Peripheral Resistance of Man

By Paul Winchell, M.D., Henry Longstreet Taylor, Ph.D., and Carleton B. Chapman, M.D.

Measurements of cardiac output and intra-arterial pressure on 5 normal young men and 5 hypertensive patients before and during sedation with Amytal demonstrated a decreased cardiac output and an increased peripheral resistance during the period of sedation. It is concluded that the theoretic basis for the use of Amytal sedation as a device for selection of hypertensive patients for sympathectomy is not valid.

Amytal, particularly its sodium salt, is known to cause a reduction in the blood pressure of some hypertensive patients. It has been assumed that the drug owes its hypotensive effect to a reduction in peripheral resistance and on this basis a Sodium Amytal test has been devised to aid in the selection of hypertensive patients for dorso-lumbar sympathectomy.1,2 Proof that the drug acts specifically to reduce the peripheral resistance is, however, lacking. Since the level of the mean blood pressure is determined by the output of the heart as well as the total peripheral resistance, it is clearly necessary to measure all three factors simultaneously in order to discern the hemodynamic action of the drug. The following experiments were designed to test existing assumptions concerning the hemodynamic action of Sodium Amytal.

Methods

Ballistocardiograms, recordings of the heart sounds, and femoral arterial pressure tracings were made simultaneously before and after the administration of Sodium Amytal to normal and hypertensive subjects. The ballistocardiograph was a low frequency, critically damped instrument of the type described by Nickerson, Warren, and Brannon.3 A strain gage and a no. 18 Courand needle were used to record the femoral pressure. Suitable hydrostatic dampers were introduced into the blood pressure recording system so that the complete recording system would pass an instantaneous square wave of 250 mm. Hg pressure with a 5 per cent overshoot. Static calibrations were carried out with a mercury manometer after every measurement of pressure. Between actual recordings the intra-arterial needle was disconnected from the strain gage and a stylet was placed in the lumen to prevent clotting.

Values for the stroke volume were determined according to the formula of Nickerson4 and the cardiac output was calculated in terms of liters per minute; ten cycles were measured for each estimation of the output. The mean blood pressure was obtained by planimetric integration of the area under the pulse wave tracing. The total peripheral resistance in dynes cm.−4 seconds was then calculated by dividing the mean blood pressure in mm. Hg by the cardiac output in cc. per second and multiplying by the factor 1332.

The subjects were 5 normotensive men between 19 and 25 years of age, and 5 men, aged between 34 and 40 years, who had essential hypertension. The mean surface areas of the two groups were 1.94 and 1.87 square meters, respectively.

Every effort was made to carry out the procedure under rigidly controlled conditions. The subjects reported to the laboratory late in the afternoon without having eaten lunch. They were placed on the ballistocardiograph table on an air mattress which was inflated during the insertion of the needle in the femoral artery and between periods of observation but which was deflated during actual observations. The temperature of the room was maintained at 24.5 ± 0.5 C., with the humidity at 50 per cent relative saturation. After the control observations were obtained, the subject received 0.40 Gm. of Sodium Amytal by mouth. An additional dose of 0.20 Gm. was given an hour later. This procedure was not followed in the case of patient G where the second and third doses were 0.4 Gm. each. This increased dosage was employed because G was known to have an increased tolerance for the drug.

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TABLE 1.—The Stroke Volume in Cubic Centimeters and the Cardiac Output in Liters per Minute of Five Normotensive and Five Hypertensive Men before and during Four Hours of Sedation with Sodium Amytal

<table>
<thead>
<tr>
<th>Subject</th>
<th>Stroke Volume, cc.</th>
<th>Cardiac Output, L./min.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hours after First Dose</td>
<td>Hours after First Dose</td>
</tr>
<tr>
<td></td>
<td>Control 1 2 3 4</td>
<td>Control 1 2 3 4</td>
</tr>
<tr>
<td>Normotensive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>131 85 100 92 80</td>
<td>10.35 6.21 7.50 6.90 5.84</td>
</tr>
<tr>
<td>B</td>
<td>123 117 85 119 144</td>
<td>7.75 5.24 4.48 6.90 9.51</td>
</tr>
<tr>
<td>C</td>
<td>117 98 91 84 75</td>
<td>7.37 6.27 5.46 5.38 5.33</td>
</tr>
<tr>
<td>D</td>
<td>118 112 124 99 119</td>
<td>7.43 6.94 5.56 8.37 8.5</td>
</tr>
<tr>
<td>E</td>
<td>124 90 87 100 96</td>
<td>7.44 5.40 4.87 5.80 5.18</td>
</tr>
<tr>
<td>Mean</td>
<td>123 96 97 99 102</td>
<td>8.07 6.01 6.37 6.36 6.74</td>
</tr>
</tbody>
</table>

Hypertensive

<table>
<thead>
<tr>
<th>Subject</th>
<th>Stroke Volume, cc.</th>
<th>Cardiac Output, L./min.</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>92 75 63 72 65</td>
<td>6.72 5.34 3.80 4.88 4.17</td>
</tr>
<tr>
<td>G</td>
<td>71 78 75</td>
<td>6.63 7.36 6.23</td>
</tr>
<tr>
<td>H</td>
<td>44 52 36 36</td>
<td>3.56 4.11 2.99 3.06</td>
</tr>
<tr>
<td>I</td>
<td>88 71 49</td>
<td>6.28 5.04 3.33</td>
</tr>
<tr>
<td>J</td>
<td>88 65 73 71 43</td>
<td>5.90 4.75 4.50 4.12 3.05</td>
</tr>
<tr>
<td>Mean</td>
<td>76 68 59</td>
<td>5.82 5.32 4.26</td>
</tr>
</tbody>
</table>

Simultaneous records of blood pressure and cardiac output were made every hour until the experiment was terminated four hours after the first dose of Sodium Amytal. In three experiments it was necessary to discontinue the procedure earlier because the subjects became restless as the sedative action of the Sodium Amytal was diminished. The majority of subjects slept soundly during the last two and one-half or three hours of the procedure. All of the subjects were sedated to the sleep level at some time during the experiment. In most instances it was possible to deflate the mattress and connect the pressure recording system without disturbing the subject.

RESULTS

In both normotensive and hypertensive groups there was a marked decrease in cardiac output which was primarily the result of a decrease in stroke volume (table 1). The decrease was roughly 20 per cent in each of the groups. The mean blood pressure remained unchanged in the control group and decreased somewhat in the hypertensive group (table 2). In both groups the total peripheral resistance rose. The Fisher T test was used to test the differences between the mean of the control period and the mean of the different time intervals after administration of Amytal. This analysis showed that the changes in cardiac output and peripheral resistance in the control group at one, two and three hours after Amytal were significant at the 5 per cent level of probability. The hypertensive group showed a somewhat larger variability. The T test indicated that the difference between the mean cardiac output in the control period and that at the end of two hours sedation closely approached the 5 per cent level of probability. The T value was found to be 2.73 while T 0.05 = 2.77. Perusal of table 2 shows that at the end of the second hour, the mean blood pressure was lower and the peripheral resistance higher than the corresponding control values in 4 of the 5 hypertensive subjects.

DISCUSSION

The results obtained do not, therefore, support the view that Sodium Amytal causes a decrease in the blood pressure of hypertensive patients by lowering the total peripheral resistance. On the contrary, the drug appears to
cause a significant increase in total peripheral resistance and a decrease in cardiac output. If the latter is sufficiently marked, a decrease in mean blood pressure results in spite of the increase in total peripheral resistance. Little or no change in mean blood pressure is seen if the changes in the two opposing effects are more or less equal. The theoretic basis for the Amytal test as a means for selecting candidates for sympathectomy seems to be highly dubious, if not invalid.

The conditions of the experiments do not, of course, duplicate those of the Amytal test as ordinarily carried out. Some of the procedures, such as femoral puncture and inflation and deflation of the air mattress, were undoubtedly somewhat disturbing to the subject. It is not likely, however, that the disturbances played a significant role in determining the nature of the experimental results. For example, the difference in the cardiac output before and after the introduction of the Courmand needle into the femoral artery was only 300 cc. and was not statistically significant. It is also apparent that under the experimental conditions a definite decrease (up to 48 mm. Hg) in the mean blood pressure was observed in all but one of the hypertensive subjects. The Sodium Amytal test as performed in the experiments was, therefore, qualitatively if not quantitatively comparable to the test as ordinarily carried out.

In view of the changes in mean blood pressure in the hypertensive subjects, it is of interest to inquire into the validity of the factors used to convert the ballistocardiographic forces to cardiac outputs determined by the ballistocardiograph correlate well with cardiac outputs determined by the Fick principle (catheterization). In this laboratory comparisons were made between duplicate measurements of the cardiac output by the acetylene method corrected to direct Fick levels and the ballistocardiograph in 18 hypertensive and 42 normotensive individuals whose ages were between 47 and 56 years. It was found that the relationship between the acetylene and the ballistocardiographic cardiac outputs did not change over a wide range of blood pressures.

The pre-Amytal cardiac outputs in the control group were somewhat higher than the comparable figures for the hypertensive group. This difference is undoubtedly related to the decrease in the cardiac output that occurs with age, the evidence for which has been recently reviewed by Tanner.

The effect of barbiturates on the cardiac output in animals has not been studied by the direct comparison of cardiac output measurements before and after administration of the drug in a manner similar to that employed in the Amytal test with man. However, in accord with the present results, there is ample evidence to demonstrate that continued barbiturate anesthesia depresses the cardiac output in dogs. For example, Shore, Holt, and Knoefel found that the cardiac output of dogs decreased by as much as 50 per cent during the first four hours of sodium barbital anesthesia. In the same animal, Blalock reported decreased cardiac output during the first 90 minutes under barbital anesthesia.

It is apparent, therefore, that barbiturates, and particularly Amytal, tend to depress the cardiac output. In the normal individual an increase in the total peripheral resistance maintains the blood pressure at normal levels. In the hypertensive patient a falling blood pressure during sedation with Amytal may merely represent the failure of the vasoconstricting mechanisms to keep pace with the decreasing cardiac output. A relative hypotension may be produced by Amytal as a result of excessive decline in cardiac output, or insufficient vasoconstriction, or both. In this small series the several possibilities are illustrated. An important decline in mean blood pressure may occur in the face of a substantial rise in the peripheral resistance. At the second hour patient 1 exhibited a fall of 58 mm. in mean blood pressure and a rise of 32 per cent in the peripheral resistance; this response is explained by a 47 per cent decline in cardiac output.

There is no evidence in any of the data presented that sedation with Sodium Amytal depresses the vasoconstrictor center or causes a relaxation of the peripheral arterioles. The
physiologic evidence, then, gives ample support to the view, as presented by de Takats, Julian and Fowler, that the Amytal test does not identify patients who are suffering from neurogenic hypertension. As a test of the ability of the peripheral arterioles to relax, there is no support whatever for the Amytal test. Conceivably, the Amytal test might be used for the very different purpose of assaying the capacity of the vessels to undergo further marked vasoconstriction (patient F), or of the heart to withstand the depressing effect of Amytal (patient G). Neither of these factors appears to have much relevance to the selection of patients for sympathectomy.

**SUMMARY AND CONCLUSIONS**

1. Five normal young men were sedated with Sodium Amytal for four hours. Simultaneous mean intra-arterial blood pressures and cardiac outputs were determined by the ballistocardiographic method during a control period and at hourly intervals after administration of Amytal.

2. Similar observations were obtained on 5 male hypertensive individuals.

3. The characteristic response in both groups was a decrease in the cardiac output and an increase in the peripheral resistance. The mean blood pressure remained unchanged in the normal group and decreased somewhat in the hypertensive group.

4. No evidence was found to show that Amytal sedation causes a relaxation of the arterioles.

5. The mechanism for the fall in blood pressure observed in hypertensives during Amytal sedation was discussed.

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**REFERENCES**


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