CARDIOVASCULAR RESPONSES TO SEVERAL ULTRA-SHORT ACTING BARBITURATES

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The main purpose of this investigation was to compare the trend of cardiac outputs by the cuvette oximeter using the single scale method of Nicholson and Wood (1) between forty and eighty minutes after the administration of sodium salts of thiopental, hexobarbital, Kemithal and thiamylal.

METHOD

Studies were made on dogs anesthetized with one of the short acting barbiturates. No preanesthesia medication was given. Immediately after the initial intravenous injection of one of the barbiturates, a tracheal cannula was inserted and the dog attached to a spirometer filled with oxygen. Inhalation of oxygen was continued throughout. Observations on cardiac output were begun after about forty minutes, and six (occasionally seven) successive determinations were made during the next forty minutes.

We attempted to maintain the dogs in the first plane of Stage III by intermittent injection of a small amount of the anesthetic agent whenever slight movement was noted. All animals maintained adequate pulmonary ventilation by spontaneous respiration. Each dog's heparinized arterial blood, after oxygen inhalation for about forty minutes, was used for calibration of the cuvette oximeter. The blood was withdrawn just before the first injection of dye. Known amounts of dye (T-1824) were added to aliquot portions of the control blood and the effect on the transmission of light in the cuvette oximeter was recorded immediately after completion of the experiment. The dye was injected into the left jugular vein, and flushed in with about 30 cc. of 0.9 per cent NaCl. The amount injected was determined by the difference in weight of the syringe before and after the injection. The amount injected was about 8 mg. each time. Immediately before each dye injection the beam of the infrared cell was adjusted to a selected point. The red and infrared cells were then bucked against each other and, in this manner, compensation for variations in the total amount of hemoglobin, as well as for residual dye, was accomplished. Femoral blood pressure was recorded by strain gauge connected in series with

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the cuvette oximeter. Electrocardiographic records were made (Lead II), immediately after each cardiac output determination, by means of a "Simpli-Scribe" Portable Model Cambridge Electrocardiograph. During the course of an experiment the animal received between 300 and 400 cc. of 0.9 per cent NaCl containing about 0.2 per cent heparin, in conjunction with injecting dye and flushing out the cuvette oximeter between determinations.

RESULTS

Fifty-seven determinations were made on 9 dogs anesthetized with thiopentonal sodium. The average dose was 9.77 mg./min./m². The range of cardiac index was 1.08–7.37, with a mean of 3.76 liters/min./m². The range of systolic blood pressure was 75–272, with a mean of 190 mm. of mercury. The range of diastolic blood pressure was 50–147, with a mean of 119. The range of mean blood pressure was 58–187, with an average of 143 mm. The range of peripheral resistance was 1842–13660, with a mean of 5205 dynes/sec./cm.². The range of heart rate was 108–244, with a mean of 194 beats per minute. The range of stroke index was 8–41, with a mean of 19 ml./beat/m².

Fifty-seven determinations were made on 9 dogs anesthetized with hexobarbital. The average dose was 20.5 mg./min./m². The range of cardiac index was 1.22–6.65, with a mean of 3.68 liters/min./m². The range of systolic blood pressure was 150–239, with a mean of 190 mm. of mercury. The range of diastolic blood pressure was 69–149, with a mean of 117 mm. The range of mean blood pressure was 99–172, with an average of 141 mm. The range of peripheral resistance was 2033–13605, with a mean of 5037 dynes/sec./cm.². The range of heart rate was 138–216, with a mean of 168 beats per minute. The range of stroke index was 9–38, with a mean of 22 ml./beat/m².

Sixty-four determinations were made on 10 dogs anesthetized with Kemithal. The average dose was 19.0 mg./min./m². The range of cardiac index was 1.14–5.63, with a mean of 3.04 liters/min./m². The range of systolic blood pressure was 91–323, with a mean of 187 mm. of mercury. The range of diastolic blood pressure was 45–158, with a mean of 109 mm. The range of mean blood pressure was 60–211, with an average of 135 mm. The range of peripheral resistance was 3022–15569, with a mean of 6127 dynes/sec./cm.². The range of heart rate was 114–240, with a mean of 172 beats per minute. The range of stroke index was 7–31, with a mean of 17 ml./beat/m².

Sixty-one determinations were made on 9 dogs anesthetized with thiamylal. The average dose was 8.36 mg./min./m². The range of cardiac index was 2.07–5.65, with a mean of 3.48 liters/min./m². The range of systolic blood pressure was 148–270, with a mean of 201 mm. The range of diastolic blood pressure was 71–152, with a mean of 123 mm. The range of mean blood pressure was 95–190, with an average of 149 mm. The range of peripheral resistance was 3154–9569, with
CARDIOVASCULAR RESPONSES TO BARBITURATES

a mean of 5872 dynes/sec./cm.$^{-2}$. The range of heart rate was 120–262, with a mean of 178 beats/min. The range of stroke index was 10–35, with a mean of 20 ml./beat/m.$^2$.

A summary of the observations on cardiovascular functions is presented in table 1. The electrocardiographic results are not included in the table. The only cardiac irregularity noted under thiopental was an occasional premature ventricular systole in 1 dog. No irregularities were noted under hexobarbital. Six of the 10 dogs receiving Kemithal exhibited cardiac irregularities. The most frequent type was a bigeminal. In 1 of the dogs receiving thiamylal every third beat was a premature ventricular systole.

<table>
<thead>
<tr>
<th>TABLE 1</th>
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<tbody>
<tr>
<td>SUMMARY OF RESULTS</td>
</tr>
<tr>
<td>THE ARITHMETIC MEANS AND STANDARD ERRORS OF ALL THE OBSERVATIONS MADE UNDER EACH BARBITURATE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Observations</th>
<th>Thiopental</th>
<th>Hexobarbital</th>
<th>Kemithal$^*$</th>
<th>Thiamylal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac index, 1/min./m.$^2$</td>
<td>3.76 ± 0.16</td>
<td>3.67 ± 0.16</td>
<td>3.04 ± 0.14</td>
<td>3.48 ± 0.11</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>190 ± 5.2</td>
<td>190 ± 2.8</td>
<td>187 ± 7.3</td>
<td>201 ± 4.5</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>119 ± 2.9</td>
<td>117 ± 2.1</td>
<td>109 ± 4.0</td>
<td>123 ± 2.6</td>
</tr>
<tr>
<td>Mean blood pressure</td>
<td>143 ± 4.0</td>
<td>141 ± 2.5</td>
<td>135 ± 5.1</td>
<td>149 ± 3.0</td>
</tr>
<tr>
<td>Peripheral resistance, dynes/sec./cm.$^{-2}$</td>
<td>5205 ± 248</td>
<td>5037 ± 304</td>
<td>6127 ± 332</td>
<td>5872 ± 227</td>
</tr>
<tr>
<td>Heart rate</td>
<td>194 ± 3.8</td>
<td>168 ± 2.6</td>
<td>172 ± 4.1</td>
<td>178 ± 4.2</td>
</tr>
<tr>
<td>Stroke index, ml./beat/m.$^2$</td>
<td>19 ± 0.8</td>
<td>22 ± 0.9</td>
<td>17 ± 1.0</td>
<td>20 ± 0.7</td>
</tr>
</tbody>
</table>

$^*$ Kemithal was supplied by Fort Dodge Laboratories, Fort Dodge, Iowa.

In order to test the variability of cardiovascular functions, a series of six (occasionally seven) successive determinations was made on each dog at approximately five minute intervals. The results found on the first determination under each barbiturate were averaged, and compared with the average results found on the sixth determination of the same dogs. About thirty-five minutes elapsed between these two sets of observations (second, third, fourth and fifth observations intervening). The difference between the first and sixth sets of observations is shown in table 2, as per cent change. It is evident that the change in heart rate was less than 5 per cent, and the changes in arterial blood pressure were less than 10 per cent (with the exception of diastolic under Kemithal).

From our results we believe that the anesthesiologist may feel confident that the condition of a patient under anesthesia is fairly constant,
TABLE 2

DIRECTION AND EXTENT OF CHANGE (IN %) BETWEEN FIRST AND SIXTH DYE INJECTIONS

<table>
<thead>
<tr>
<th></th>
<th>Cardiac Index</th>
<th>Systolic Blood Pressure</th>
<th>Diastolic Blood Pressure</th>
<th>Mean Blood Pressure</th>
<th>Peripheral Resistance</th>
<th>Heart Rate</th>
<th>Stroke Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thioental</td>
<td>+25.1</td>
<td>-7.6</td>
<td>-6.4</td>
<td>-6.7</td>
<td>-19.4</td>
<td>-4.1</td>
<td>+23.5</td>
</tr>
<tr>
<td>Hexobarbital</td>
<td>+36.8</td>
<td>-2.1</td>
<td>-4.4</td>
<td>-2.9</td>
<td>-31.0</td>
<td>-2.9</td>
<td>+47.0</td>
</tr>
<tr>
<td>Kemithal</td>
<td>+51.7</td>
<td>+2.2</td>
<td>-11.9</td>
<td>-5.0</td>
<td>-41.6</td>
<td>+1.2</td>
<td>+53.8</td>
</tr>
<tr>
<td>Thiamylal</td>
<td>+29.4</td>
<td>-1.5</td>
<td>-2.4</td>
<td>-2.0</td>
<td>-22.4</td>
<td>+4.1</td>
<td>+29.4</td>
</tr>
</tbody>
</table>

The change which occurred between the first set of observations and the sixth, about 35 minutes later, in the same dogs is indicated. Although the changes in heart rate and blood pressure are small, those in cardiac index, peripheral resistance and stroke index are large.

as judged by blood pressure and pulse rate, but there may be marked changes in cardiac output, stroke volume and peripheral resistance. The cardiac index changed least under thioental and most under Kemithal. The same is true for peripheral resistance and stroke index.

DISCUSSION

The cuvette oximeter permits determinations of cardiac output without the introduction of cardiac catheters. It permits repeated determinations in animals within a short period of time, therefore, the trend of cardiovascular functions during the course of anesthesia may be ascertained. It permits the use of any type of anesthetic agent. The results found by cuvette oximeter correlate well with the Stewart spectrophotometric method (2). The error inherent in the method is of the same magnitude as that of the direct Fick, namely, about 11 percent (1). The values found for cardiac index by cuvette oximeter under the ultra-short acting barbiturates are within the range found in unanesthetized dogs by the Fick method (3, 4). Vidt et al. (5) found canine cardiac outputs highly unstable in both anesthetized and unanesthetized dogs by the rose bengal method.

During the course of thioental anesthesia the cardiac index increased, in contrast to the results found by other observers in patients. In patients who had received two or more preanesthesia medication agents, and then thioental, the cardiac index decreased (6–9). It is difficult to evaluate the effect exerted by the variety of preanesthesia medication agents used in the patients. The reason for the increase in the cardiac output in our experiments during the period of anesthesia is not known. It is not likely to be due to the repeated injection of dye; if this were the cause, the increases would be comparable regardless of the anesthetic agent used. From the results of others it does not seem to be due to an increase in central venous pressure (7–10). A decreasing anesthetic concentration in the blood seems not to be the factor of
importance, since in an earlier study (11) the cardiac output increased during thiopental anesthesia in spite of an increase in concentration of thiopental in the blood. There is undoubtedly a relationship between the increase in cardiac output and the decrease in total peripheral resistance during the course of anesthesia, and it is probable that vasodilatation is a factor of prime importance in permitting a larger output. The total peripheral resistance in this series is higher than that reported by Bing (3) for the unanesthetized dog, but within the range reported by others under various anesthetic agents (12-15). The total peripheral resistance decreased during the period of observation of this series (forty to eighty minutes after administration of the barbiturate).

The cardiac irregularities observed were not due to hypoxia. The oxygen saturation was determined in 9 of the dogs; it varied from 95.2 to 100 per cent, with a mean of 98.5 per cent at the time of the first dye injection and 98.6 per cent at the time of the last. The frequency of cardiac irregularities under Kemithal was not surprising in view of the fact that similar results have been found in patients (16).

There was no evidence of carbon dioxide retention. The range of carbon dioxide content at the time of the first dye injection was 32.7 to 52.5, with a mean of 40.9 volumes per cent. At the time of the last dye injection the range was 30.2 to 44.7, with a mean of 35.6 volumes per cent. No determinations of pH were made, so carbon dioxide tension values are not available.

**Summary**

The cardiac index and stroke index increase markedly during the course of anesthesia under short acting barbiturates in dogs. The total peripheral resistance decreases.

A rough comparison indicates the following order of effectiveness in dogs: thinamylal, thiopental, Kemithal and hexobarbital. From the cardiovascular standpoint thiopental is most satisfactory and Kemithal least so.

Despite a fairly steady pulse rate and blood pressure, the cardiac output, stroke volume and total peripheral resistance can undergo marked changes in dogs.

**References**


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