INFLUENCE OF CHLORPROMAZINE ON SURVIVAL TIME OF SHOCKED RATS

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Because of reports which indicated that there might be value in the use of chlorpromazine to offset many of the deleterious effects of shock (1, 2, 3), it was decided to use that drug in rats which had received a standard traumatic shock (4) to see whether information could be obtained experimentally concerning the value of chlorpromazine. It also was thought that the head-up position which would tend to drain blood away from the vital centers if any sort of ganglionic block were produced by chlorpromazine should be used to further test the value of chlorpromazine.

METHODS

Fifty albino rats of the Charles River strain (groups A, B, C, and D) and of approximately the same weight (200 ± 10 Gm.) were anesthetized with cyclopropane and put in a plaster of Paris cast. The cyclopropane was allowed to flow with twice its volume of oxygen into a 200 cc. chamber into which the head of the animal was inserted with a snug sponge collar. The jugular vein was cannulated and heparin injected so that blood pressures could be obtained. The rats were allowed to awaken. The cast prevented tearing out the cannulas during exposure of the cecum and circumvented the need for anesthesia during such exposure. The animals were then given a standard trauma which consisted of light pinches of the cecum 3 times per second for 15 minutes, using a hemostatic forceps having 2 cm. jaws. Thirty of these animals (groups C and D) were left supine and 20 (groups A and B) were tilted in a 45 degree head-up position. Ten of the 20 tilted animals (group B) and another 10 (group D) of the 30 supine animals were given chlorpromazine 2.5 mg./kg. intravenously. No anesthetic agent was given thereafter and survival times were noted. Tracheostomies were not done with these animals because they struggled so that a tracheal cannula probably would have been pulled out or the trachea torn. In view of the struggling, it seemed likely that these animals were traumatized at least as much as the noncast animals who were treated as described below.

Seventy rats of the same strain and the same weight range were anesthetized with ether (groups E, F, G, H, J, K, and L). They were heparinized and the carotid artery and the jugular vein were cannulated and tracheostomies were done. The animals were then given

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the standard trauma. Twenty of these animals (groups E and F) were tilted 45 degrees head-up. Ten of the animals that were tilted (group F) were given chlorpromazine 2.5 mg./kg. intravenously. All 20 continued to receive ether in amounts just sufficient for surgical anesthesia until they expired. The criterion of sufficiency of surgical anesthesia was lack of response to a pinch of the ankle with a hemostat. Another 20 (groups G and H) of the 70 animals were treated similarly to the first 20 except that they were left supine.

The ether was given drop by drop into a 200 cc. chamber into which flowed oxygen or air and from which the vapor flowed to the tracheostomy tube of the animals. Ether therefore was given on demand by the animal as is done clinically with patients. Ether-oxygen and ether-air flows gave results with no significant difference. Group G was considered to be an ether control group without tilt and without chlorpromazine. The remaining 30 (groups J, K, and L) of the 70 etherized rats were given chlorpromazine 2.5 mg./kg. intravenously following the trauma. All were left supine. Ten (group K) of the 30 received cyclopropane for surgical anesthesia. Cyclopropane was given in the same 200 cc. chamber into which the ether had been introduced. Cyclopropane was introduced as a 33 per cent concentration; it ran only a very small proportion of the time. Again, this was administered in the same fashion as would have been done clinically. Ten rats (group L) received thiopental for anesthesia. The thiopental was given intravenously as a 1 per cent solution, using 0.05 cc. at each administration. The amounts required in the approximately 3 hour period varied between 0.15 cc. (1.5 mg.) and 0.8 cc. (8 mg.). Survival times were noted.

Results

In table 1, comparison of groups A with C, B with D, E with G, and F with H indicates that the 45 degree head-up tilt was followed by no significant effect on survival time as compared with those that were not tilted. Comparison of groups A with B, C with D, E with F, and G with H indicates that administration of chlorpromazine following trauma had no significant effect on survival time. The average survival time of the animals in group G which received ether with oxygen was 150 minutes. The average obtained for 10 rats given ether in air (not listed in the table) was 155 minutes. Blood pressure curves obtained during and following trauma gave the same comparative values here that they did in a previous report (5). As observed earlier, when increments of anesthetic agent consisting of ether or thiopental were given to the traumatized subjects, the blood pressure continued to fall consistently. When cyclopropane was the agent used, the blood pressure showed a tendency to rise after each administration of the anesthetic agent. It eventually fell because of the trauma.
TABLE 1
INFLUENCE OF ANESTHETIC AGENT, OR 45 DEGREE TILT, AND OF CHLORPROMAZINE ON SURVIVAL TIME OF SHOCKED RATS

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Rats</th>
<th>Agent for Induction</th>
<th>Trauma Here</th>
<th>Position After Shock</th>
<th>Chlorpromazine 2.5 mg./kg. After Shock</th>
<th>Anesthetic Agent After Shock</th>
<th>Average Survival Time (Minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>10</td>
<td>Cyclopropane for east</td>
<td>Awake</td>
<td>45° head-up</td>
<td>No</td>
<td>None</td>
<td>None</td>
<td>152</td>
</tr>
<tr>
<td>B</td>
<td>10</td>
<td>Cyclopropane for east</td>
<td>Awake</td>
<td>45° head-up</td>
<td>Chlorpromazine</td>
<td>None</td>
<td>None</td>
<td>153</td>
</tr>
<tr>
<td>C</td>
<td>20</td>
<td>Cyclopropane for east</td>
<td>Awake</td>
<td>Supine</td>
<td>No</td>
<td>Chlorpromazine</td>
<td>None</td>
<td>134</td>
</tr>
<tr>
<td>D</td>
<td>10</td>
<td>Cyclopropane for east</td>
<td>Awake</td>
<td>Supine</td>
<td>Chlorpromazine</td>
<td>No</td>
<td>Ether</td>
<td>164</td>
</tr>
<tr>
<td>E</td>
<td>10</td>
<td>Ether</td>
<td>Ether</td>
<td>45° head-up</td>
<td>No</td>
<td>Chlorpromazine</td>
<td>Ether</td>
<td>137</td>
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<tr>
<td>F</td>
<td>10</td>
<td>Ether</td>
<td>Ether</td>
<td>45° head-up</td>
<td>Chlorpromazine</td>
<td>Ether</td>
<td>No</td>
<td>142</td>
</tr>
<tr>
<td>G</td>
<td>10</td>
<td>Ether</td>
<td>Ether</td>
<td>Supine</td>
<td>No</td>
<td>Chlorpromazine</td>
<td>Ether</td>
<td>150</td>
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<td>H</td>
<td>10</td>
<td>Ether</td>
<td>Ether</td>
<td>Supine</td>
<td>Chlorpromazine</td>
<td>Ether</td>
<td>No</td>
<td>146</td>
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<tr>
<td>J</td>
<td>10</td>
<td>Ether</td>
<td>Ether</td>
<td>Supine</td>
<td>Chlorpromazine</td>
<td>Ether</td>
<td>No</td>
<td>193</td>
</tr>
<tr>
<td>K</td>
<td>10</td>
<td>Ether</td>
<td>Ether</td>
<td>Supine</td>
<td>Chlorpromazine</td>
<td>Cyclopropane</td>
<td>Thiopental</td>
<td>183</td>
</tr>
<tr>
<td>L</td>
<td>10</td>
<td>Ether</td>
<td>Ether</td>
<td>Supine</td>
<td>Chlorpromazine</td>
<td>Thiopental</td>
<td>No</td>
<td>200</td>
</tr>
</tbody>
</table>

H-J  p < 0.05  T = 70  A-B  C-D  Not significant
H-K  p < 0.02  T = 74  A-C  G-H  Not significant
H-L  p < 0.01  T = 67  B-D  J-K  Not significant

* Wilcoxon's T.

An interesting result occurred which may be seen when one compares the survival times of groups H, J, K, and L. Those animals that received ether had a significantly shorter survival time than the animals that received no anesthetic agent or that received cyclopropane or thiopental following the trauma.

DISCUSSION

The authors are unaware of objective data which would indicate that chlorpromazine is beneficial when given subsequent to traumatic shock. However, there are inferences (1, 2, 3) that such might be the case. This could be of extreme importance in case of war. These experiments uncover no benefit to be obtained from giving chlorpromazine under these circumstances where the results were based on survival time. If chlorpromazine were truly ganglioplegic, it might be expected that blood would pool in dependent areas so the head-up position might be expected to be deleterious to vital centers. The results show no inimical effect on survival time.

Chlorpromazine has been reported to lessen the quantity of anesthetic agent required for surgical anesthesia (6). In these experiments, the 3 commonly used anesthetic agents—ether, cyclopropane, and thiopental—were given to different groups of rats in amounts just sufficient to obtain surgical anesthesia following shock and chlor-
promazine. It was easily apparent that less anesthetic agent was required for animals that had received chlorpromazine than for animals that had not received this drug. Cyclopropane and thiopental provided adequate analgesia with no significant change in survival time, but, when ether was used as the anesthetic agent, there was a statistically significant shorter survival time. This latter observation is in accord with results reported earlier (5) concerning the effect of anesthetic agents on survival time of shocked rats. In those experiments, ether did not permit as long survival period as did cyclopropane or thiopental.

These experiments have no bearing on situations in which chlorpromazine might be given prior to shock. Such experiments were not done because clinical application obviously would be impractical.

It will be noted that no direct comparisons are made here between the nontracheotomized groups (A through D) and those that did have tracheostomies (groups E through L).

SUMMARY

Standardized trauma which resulted in 100 per cent fatality and in reasonably consistent survival periods was administered to 120 rats which were (a) awake or asleep, (b) supine or tilted, (c) given chlorpromazine after trauma or not and (d) anesthetized with ether, cyclopropane, or thiopental, or not anesthetized following trauma.

No significant change in survival time was observed due to chlorpromazine or to head-up tilt.

Shocked animals given chlorpromazine which received ether afterward survived for shorter periods than did those getting cyclopropane or thiopental.

ACKNOWLEDGMENT

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REFERENCES