THE EFFECTS OF LARGE DOSES OF BARBITURATES AND MORPHINE AND SCOPOLAMINE ON RESPIRATORY MINUTE VOLUME EXCHANGE

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Received for publication October 4, 1948

INTRODUCTION

Nitrous oxide and ethylene are anesthetic agents which possess a common disadvantage, that of relative impotence. Considerable debate, research, clinical trials and controversy have marked the attempts through the years to circumvent this common deficiency. The use of these agents with insufficient concentrations of oxygen has been condemned and largely abandoned by most anesthesiologists in this country. It is possible, however, to use these agents to advantage by prior or concurrent depression of reflex irritability and metabolism with the barbiturates, and morphine and scopolamine in varying, but relatively heavy, doses. With the assistance of the heavy medication, nitrous oxide and ethylene can produce good first plane anesthesia without reduction in the oxygen concentration to undesirable levels.

In using heavy premedication to obtain anesthesia with these agents, one is concerned with the effect on the respiratory mechanism as reflected in the patient’s tidal volume and minute volume exchange. How severely are these values depressed by the usual doses of heavy premedication?

In an attempt to determine, at least in part, the answer to this question, the study about to be described was undertaken.

METHODS

The patients selected included those who were to undergo operations for which nitrous oxide or ethylene would fulfill the requirements. Most of these procedures were of a superficial nature requiring little

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or no relaxation and yet of fairly long duration. Such procedures included radical mastectomies, vaginal plastic operations, skin grafts with plastic reconstruction, and high saphenous ligations with multiple excisions. Thirty such patients were studied for this series.

Premedication of the heavy type was accomplished in this study with pentobarbital, morphine and scopolamine. Pentobarbital offers excellent hypnosis and acts synergistically with morphine and scopolamine to provide a fairly uniform degree of depression (1–3). Morphine is quite predictably reliable in producing a reduction in reflex irritability, a reduction in metabolic rate and analgesia. The respiratory depression produced by morphine is counterbalanced to a certain extent by scopolamine. This belladonna derivative also contributes a useful degree of psychic sedation and amnesia. Morphine and scopolamine were given in the conventional 25 to 1 ratio as recommended by Waters, Hawk and Wangeman (4, 5).

Dosage ranges in this study were as follows: for healthy individuals between the ages of 12 and 60 years, pentobarbital 180 mg., morphine 10 mg., and scopolamine 0.43 mg.; between the ages of 60 and 75 years, pentobarbital 90 mg., morphine 8 mg., and scopolamine 0.33 mg.

The route and time of administration in the majority of the patients was as follows: pentobarbital by mouth two hours prior to induction of anesthesia, and morphine and scopolamine hypodermically one and a half hours prior to induction. In those situations in which the time of induction was indeterminate, all of the premedication was administered intravenously fifteen to twenty minutes before induction of anesthesia.

In instances in which it was anticipated that operation would be two to four hours in duration, a second dose of morphine and scopolamine was usually given intravenously in amounts approximately two-thirds the initial dose. This was administered just before induction, subject to the apparent need as exhibited objectively by the patient. Anesthesia was induced and maintained with the anesthetic machine delivering approximately 70 per cent nitrous oxide or ethylene and 30 per cent oxygen. Nearly all of the anesthetics were administered using the absorption circle filter with a semiclosed technic.

Spirometer tracings were obtained with a Benedict-Roth metabolism machine with outside flutter valves. The resistance to breathing of this machine approximated that of the absorption circle filter. Readings were taken on each patient on three different occasions. The first was usually taken the day before operation when the procedure was outlined to the patient. This afforded an opportunity for the patient to accustom himself to the mask and machine and in part mitigated the possibility of an apprehensive and exaggerated type of respiration. The reading obtained at this point was designated as a control.

The second reading was obtained when the depressant effect of the premedication was maximal, that is, just prior to the induction of anesthesia. This was two hours after pentobarbital given orally and one
and a half hours after morphine and scopolamine given by hypodermic injection or fifteen to twenty minutes after all premedication had been given intravenously.

The third reading was taken during anesthesia after the first plane of third stage was definitely reached. The control and the post-premedication readings were taken with the patient breathing air from the spirometer. The reading taken during anesthesia was made with the spirometer containing the anesthetic mixture being used. From these readings the tidal volume and the minute volume exchange were calculated.

**Results**

The mean tidal volumes were determined for each of the three readings. The post-premedication reading and the reading taken during anesthesia were then compared with the control mean. The post-premedication mean tidal volume was found to be 67.9 per cent of the control mean and the mean during anesthesia was found to be 60.1 per

<table>
<thead>
<tr>
<th>TIDAL VOLUME</th>
<th>No.</th>
<th>Mean (± SD)</th>
<th>Significance Ratio (t value between)</th>
<th>Level of Significance</th>
<th>Percent of Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control TV$_1$</td>
<td>30</td>
<td>715 (± 199)</td>
<td>TV$_1$ and TV$_2$ = 7.3</td>
<td>0.1 %</td>
<td>100.0 %</td>
</tr>
<tr>
<td>TV$_2$, After Premedication</td>
<td>30</td>
<td>486 (± 135)</td>
<td>TV$_1$ and TV$_2$ = 9.4</td>
<td>0.1</td>
<td>67.9</td>
</tr>
<tr>
<td>TV$_3$, During Anesthesia</td>
<td>30</td>
<td>430 (± 93)</td>
<td>TV$_2$ and TV$_3$ = 1.8</td>
<td>10.0</td>
<td>60.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MINUTE VOLUME EXCHANGE</th>
<th>No.</th>
<th>Mean (± SD)</th>
<th>Significance Ratio (t value between)</th>
<th>Level of Significance</th>
<th>Percent of Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control MVE$_1$</td>
<td>30</td>
<td>10397 (± 3364)</td>
<td>MVE$_1$ and MVE$_2$ = 3.416</td>
<td>0.1 %</td>
<td>100.0 %</td>
</tr>
<tr>
<td>MVE$_2$, After Premedication</td>
<td>30</td>
<td>7821 (± 2273)</td>
<td>MVE$_1$ and MVE$_2$ = 3.427</td>
<td>0.1</td>
<td>75.0</td>
</tr>
<tr>
<td>MVE$_3$, During Anesthesia</td>
<td>30</td>
<td>7933 (± 1922)</td>
<td>MVE$_2$ and MVE$_3$ = 0.205</td>
<td>&gt;20.0</td>
<td>76.3</td>
</tr>
</tbody>
</table>

**Table 1**

The upper half of the table is concerned with the findings in regard to tidal volume; the lower half concerns minute volume exchange.

TV$_1$, represents the control tidal volume.

TV$_2$, represents the tidal volume after premedication.

TV$_3$, represents tidal volume during anesthesia.

MVE$_1$, represents the control minute volume exchange.

MVE$_2$, represents the minute volume exchange after premedication.

MVE$_3$, shows minute volume exchange during anesthesia.
cent of control. These values point out a significant reduction in tidal volume.

The variation of the minute volume exchange also showed a reduction, but to a lesser extent. The mean minute volume exchange after premedication was 75 per cent of the control mean. The mean during anesthesia was 76.3 per cent of the control mean. These values clearly demonstrated that the respiratory depression as reflected in the tidal volume was in part compensated for by an increase in respiratory rate. All data were subjected to statistical analysis (see table 1) and proved to be statistically significant.

**Discussion**

The clinical evaluation of this technic of administering nitrous oxide or ethylene merits a brief discussion in view of the above findings. It has been found that most any type of patient tolerates this method quite well. It is particularly adaptable to the elderly poor risk patient. Neither induction nor awakening from anesthesia was noticeably retarded due to the reductions in tidal volume or minute volume exchange. Both of these agents produce a minimum of physiologic changes when administered with ample oxygen. The more profound physiologic deviations accompanying prolonged administration of more potent agents such as cyclopropane and ethyl ether are reduced. Most of the patients are in full possession of their reflexes upon leaving the operating theater and most of them are capable of responding to vocal instructions in a matter of minutes after anesthesia has been discontinued. Nausea and emesis postoperatively are extremely infrequent.

Should the surgical procedure be of a much shorter duration than anticipated, the patient will return to his room in a moderately depressed state. This obvious difficulty can be largely avoided by careful patient selection. An occasional patient may be excessively depressed by his premedication. This infrequent difficulty can be minimized by administering the final portion of the premedication intravenously just prior to operation.

**Summary**

A study of 30 patients was made with regard to depression of tidal volume and minute volume exchange of the respiration encountered in using large doses of preoperative medication. This type of preanesthetic sedation is one method of administering nitrous oxide or ethylene in well-oxygenated mixtures.

The reduction of tidal volume occasioned by this type of premedication is in part compensated for by an increase in respiratory rate, thereby lessening the reduction in minute volume exchange.

Some of the advantages and disadvantages of this type of anesthesia have been discussed.
REFERENCES


PRELIMINARY PROGRAM

1949 ANNUAL MEETING OF THE AMERICAN SOCIETY OF ANESTHESIOLOGISTS, INC.

HOTEL NEW YORKER, NEW YORK CITY

DECEMBER 7–10, 1949

WEDNESDAY, DECEMBER 7, 1949

Morning: Meeting of the Board of Directors.

Afternoon: Program sponsored by Committee on Medical Schools and Postgraduate Education covering such non-scientific subjects as organization of departments of anesthesiology, postgraduate training, training of part-time anesthesiologists, Society programs and many other allied subjects.

THURSDAY, DECEMBER 8, 1949

Morning: Meeting of the House of Delegates.

Afternoon: Scientific session.

Dinner: Board of Governors of the American College of Anesthesiologists.

Evening: Scientific session.

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