

THE EFFECTS OF NEMBUTAL (SODIUM PENTOBARBITAL) AND SCOPOLAMINE ON HUMAN SUBJECTS*

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A previous paper was concerned with "The Effects of Morphine, Atropine and Scopolamine on Human Subjects" (1). Queries have often been raised as to the probable findings if a barbituric acid derivative were substituted for morphine in a similar study. It is hoped that this report will, in part at least, answer those queries.

The results of the previous study (1) justified the conclusion that morphine slowed the pulse rate and respiratory rate, decreased the minute volume exchange and the oxygen consumption. It was also concluded that these effects could be favorably modified when scopolamine was combined with morphine in the ratio of 1 to 25. Atropine was a less satisfactory corrective. The question has been raised as to whether barbiturates have a similar effect to that of morphine, and whether scopolamine added to a barbiturate would be similarly beneficial. Nembutal (sodium pentobarbital) was chosen because of its popularity and its pleasant effects on most subjects. The effect of the oral administration of this drug was studied alone and in combination with scopolamine hydrobromide given hypodermically. The experimental method was identical to that described in detail in the previous publication (1). With the subject at basal conditions, the body temperature, size of pupil, pulse rate and blood pressure were noted; and by means of spirometric tracings, the respiratory rate, tidal volume, minute volume and oxygen consumption were determined before and after the administration of the drugs. Observations were made from forty-five minutes before until six hours after the administration of the drugs. Nembutal grains iii was used alone, and in combination with scopolamine grain 1/100 (0.65 mg.). The effects of scopolamine grain 1/100 were observed in the previous study (1) and are reproduced here in figure 1. The same individuals served as subjects, except that (b) and (c) of the original work were replaced by subjects (f) and (h) in these experiments (fig. 2). No spirometric tracings with scopolamine alone for subjects (f) and (h) are available for comparison. It is assumed that their records would have been similar to the average.

Nembutal.—The effects of 3 grains of nembutal on the circulatory and respiratory functions of 5 individuals were fairly constant (fig. 2). Although individual variations were in some instances quite wide, in no

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instance did they continue to run contrary to the trend of the group of subjects. These trends are shown as averages in figures 5, 6, 7, 8 and 9. The pulse rate was increased moderately in the group of subjects. One

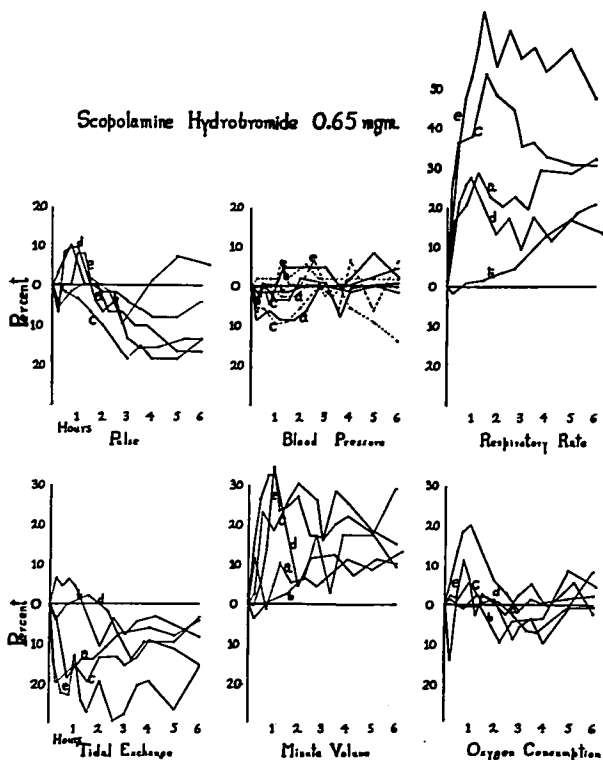


FIG. 1. Effects of scopolamine on 5 individuals. The ordinate represents percentage above or below the control level and the abscissa the number of hours after administration. The pulse rate was slightly increased during the first ninety minutes, but following this the trend was toward a decrease of about 10 per cent, with slight evidence of recovery at six hours. Both the systolic and diastolic blood pressure changes were minimal. Respiratory rate was definitely increased in all individuals and there was marked variation in individual response. Changes in tidal exchange were more subdued, but the individual who exemplified rapid rate showed the greatest decrease in tidal exchange. Minute volume was increased during the first fifteen minutes and the effect was sustained for the six hour period. Approximate oxygen consumption fluctuated early, but after two hours the changes were minimal.

subject (*h*) had a 40 per cent increase at fifteen minutes and varied from 10 to 30 per cent during the entire experiment. The drug produced a general depression of blood pressure and affected the diastolic more than the systolic pressure. The average of the respiratory rates showed an increase throughout the experiment. There was a marked decrease of respiratory rate early in the experiment in one subject (*f*) and an increase

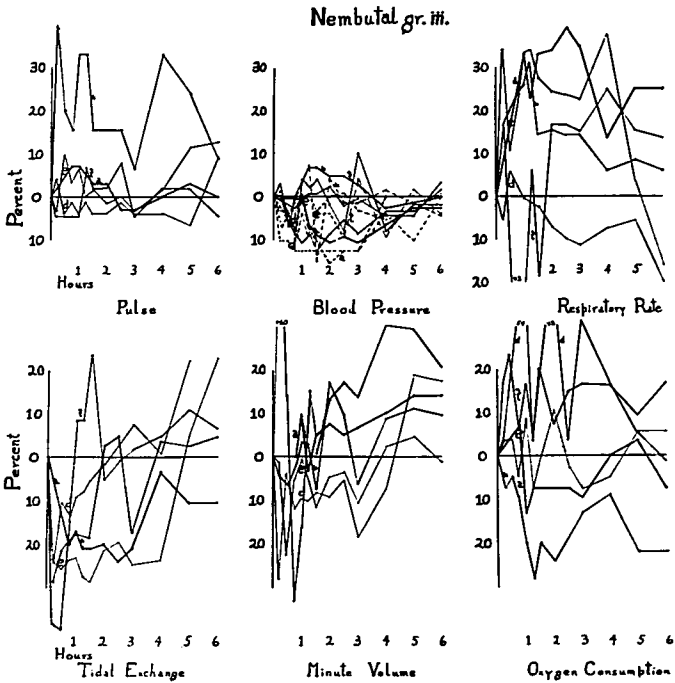


FIG. 2. The effects of nembutal on the same 5 individuals as in figure 1 except that subjects (*b*) and (*c*) were substituted for by subjects (*f*) and (*h*). The pulse rate remained relatively stable in all subjects except one (*h*) whose rate had a 40 per cent increase at fifteen minutes and varied from 10 to 30 per cent during the remainder of the experiment. The average of the effects on pulse rate (fig. 5) showed a moderate increase throughout the experiment. There was a decrease of both systolic and diastolic blood pressures. Respiratory rate was definitely increased by the drug in 3 subjects, gradually decreased in another and a wide variation in the other. Tidal exchange was decreased until the last half of the experiment when it rose to above the control level in all but 1 subject. Minute volume was decreased early in the experiment in all but 1 subject, but by the fourth hour it was above the control level. There was a wide variation of oxygen consumption but an average of the effects (fig. 9) shows that there was a small relative change.

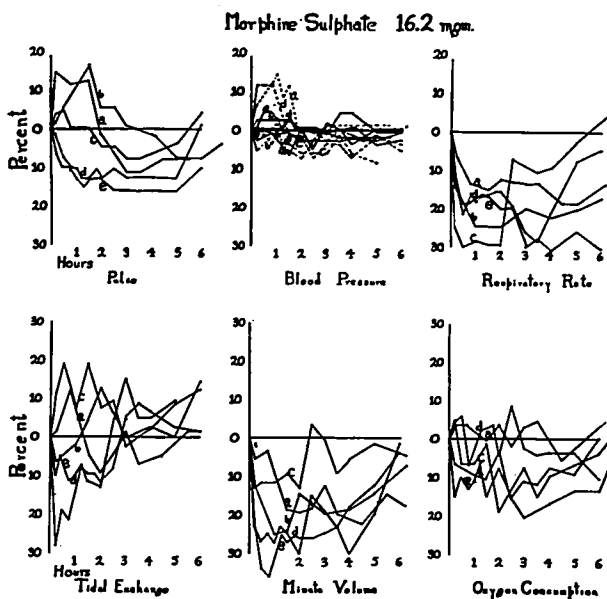


FIG. 3. Effects of morphine on the 5 subjects used in the original work. For the first ninety minutes after the injection, the pulse showed an individual response, some increased as much as 15 per cent; others decreased, but after this time interval, the trend in all cases was toward at least 10 per cent reduction of pulse rate followed by a rather sudden return to normal between the fifth and sixth hour. Diastolic blood pressure showed fluctuations for the first hour and a half, then all the changes became minimal. In all individuals the respiratory rate showed immediate marked depression with little evidence of recovery until the fourth hour, when gradual improvement was noted. Tidal exchange showed considerable variation until the third hour when the trend was slightly above the control values. Minute volume became immediately depressed as much as 35 per cent with little evidence of recovery until the fifth or sixth hour. Approximate oxygen consumption was uniformly depressed for all subjects, although of a mild degree.

later; while another (*d*) showed a gradual decrease of rate. Tidal exchange and minute volume both showed a depression until about the third hour when there was a gradual recovery to slightly above the control level. Oxygen consumption was modified only to a small degree after the administration of nembutal.

Nembutal with Scopolamine.—With the combination of nembutal and scopolamine (figs. 4, 5, 6, 7, 8, 9) there was a greater initial stimulation of the pulse rate, and then definite slowing beginning with the second hour. Respiratory rate was faster while the tidal exchange was less when

scopolamine was added to nembutal. This relationship of respiratory rate and tidal exchange resulted in a sustained increase in minute volume. Oxygen consumption was increased to a greater extent by the combination of drugs than with nembutal alone. This was no doubt due to a certain amount of restlessness caused by the scopolamine.

The objective and subjective observations during this experimental study were most interesting. All 5 subjects were objectively more restless but subjectively more comfortable with the combination of drugs than with either drug alone. Four of the 5 subjects were more cooperative

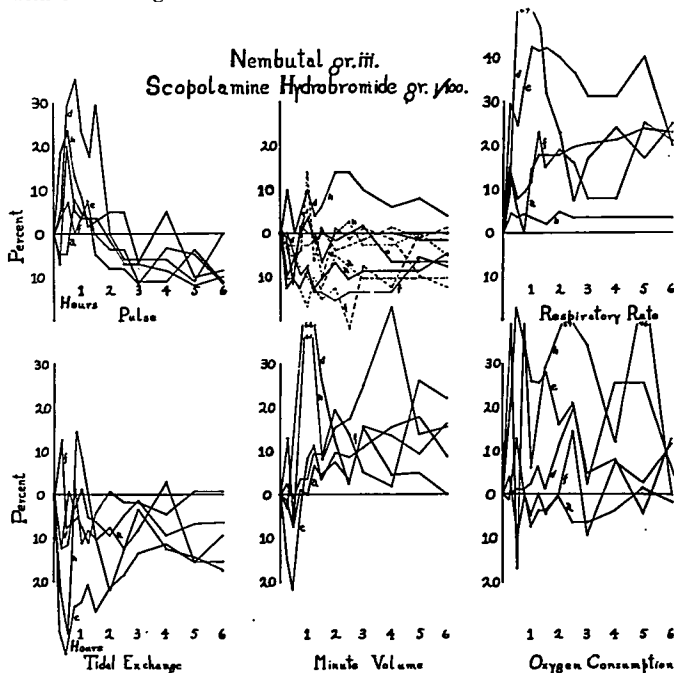


FIG. 4. Effects of the combination of nembutal and scopolamine on the same subjects as in figure 2. There was an early increase of pulse rate, greater than with either drug alone, and by the third hour all values had decreased to below the control level. A wider variation of systolic and diastolic blood pressure was noted with the combination of drugs. Respiratory rate was not increased as much by the combination as it was with scopolamine alone, but more than with nembutal alone. There was a decrease of tidal exchange, except in the first hour in one subject. Minute volume was increased by all subjects except in the first hour. Only one subject showed a sustained decrease of oxygen consumption while the others showed an average increase of from 5 to 20 per cent (fig. 9).

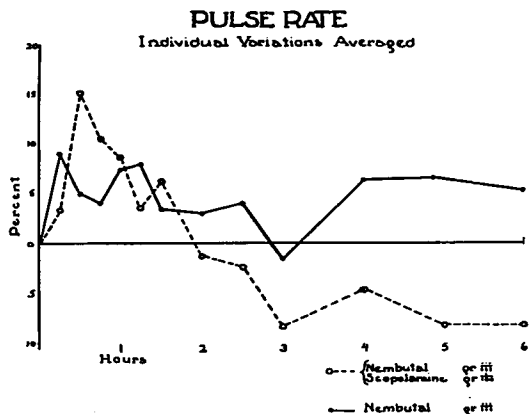


FIG. 5. A comparison of the average effects on pulse rate by nembutal and the combination of nembutal and scopolamine. Nembutal caused a moderate increase of pulse rate throughout the experiment except for a slight decrease at the end of the third hour. The combination of drugs caused a greater initial increase but by the third hour there was a decrease to below the control level for the remainder of the experiment.

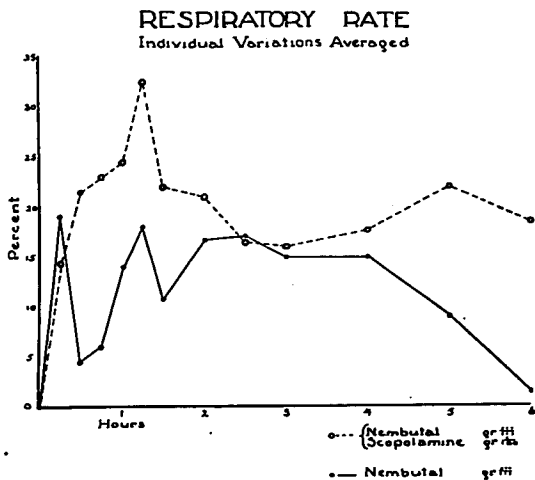


FIG. 6. A comparison of the average effects on respiratory rate by nembutal and the combination of nembutal and scopolamine. The increase of respiratory rate was greater with the combination of drugs than with nembutal alone.

and tolerant of the experimental method with the combination than with nembutal alone. One subject was so uncooperative with nembutal that the thirty minute and forty-five minute spirometric tracings could not be made. The mental depression was less with the combination than with

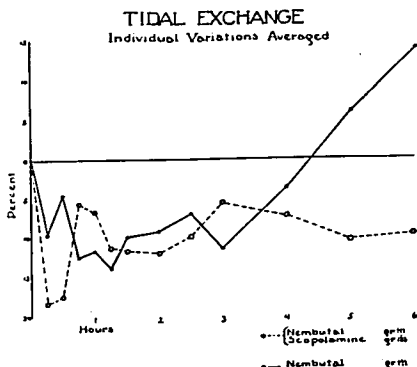


FIG. 7. A comparison of the average effects on tidal exchange by nembutal and the combination of nembutal and scopolamine. The early decrease of tidal exchange was greater with the combination of drugs than with nembutal alone, and this decrease with the combination was sustained for the remainder of the experiment, whereas with nembutal it rose above the control level during the fifth hour.

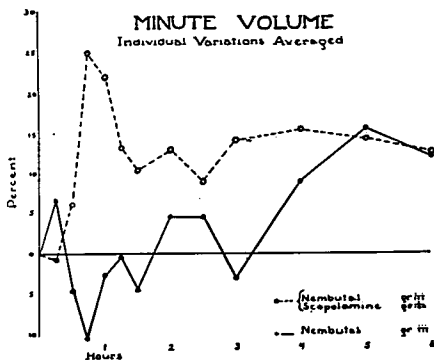


FIG. 8. A comparison of the average effects on minute volume by nembutal and the combination of nembutal and scopolamine. The effect of nembutal on minute volume was varied until the fourth hour when it was increased for the remainder of the experiment. The combination of drugs caused an increase of minute volume throughout the experiment.

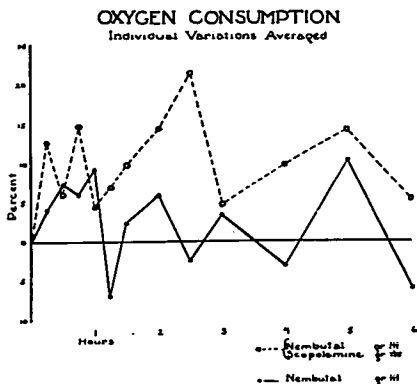


FIG. 9. A comparison of the average effects on oxygen consumption by nembutal and the combination of nembutal and scopolamine. Oxygen consumption was relatively unaffected by nembutal and increased 5 to 20 per cent by the combination of drugs.

nembutal alone, but more than that exhibited with scopolamine alone. The recovery period was definitely longer with the combination. This was due, in part at least, to the visual disturbances of the scopolamine. Dilatation of the pupils and some visual blurring were noted with the combination. There were no visual changes with nembutal. Body temperature remained almost constant during the experiments. One subject was nauseated upon arising at the conclusion of the experiment in which the combination had been administered.

DISCUSSION

Comparison of the effects of nembutal and morphine shows that, in general, 3 grains of nembutal causes less depression of respiration and circulation than does 1/4 of a grain of morphine (1). Nembutal (fig. 2) caused an increase of pulse rate about equal to the decrease caused by morphine (fig. 3). Both drugs produced a slight fall of blood pressure. The respiratory rate was decreased 10 to 30 per cent by morphine, whereas nembutal caused an increase of 2 to 18 per cent. Tidal exchange was similarly changed by both drugs; a decrease for the first two to three hours, then a gradual increase to the sixth hour. Minute volume was decreased 20 per cent by morphine and 10 per cent by nembutal. At the beginning of the third hour, however, there was a gradual increase of minute volume with nembutal to 10 per cent above the control value, whereas with morphine it remained below the control level. Oxygen consumption was decreased 5 to 8 per cent with morphine, and slightly

increased with nembital. Such changes appear to depend upon modification of muscular activity.

Either the combination of morphine and scopolamine or of nembital and scopolamine (fig. 4) has a similar effect on pulse rate and blood pressure. Minute volume exchange is decreased with morphine and scopolamine, and increased with nembital and scopolamine. Morphine and scopolamine had very little effect on oxygen consumption, while nembital and scopolamine caused a 5 to 20 per cent increase. Changes in oxygen consumption appeared to depend upon variations in muscular tone and activity.

Clinical Use of Nembital and Scopolamine.—Nembital grains iii and scopolamine grain 1/100 administered one and one-half hours before operation provided pleasant and adequate psychic sedation as well as mucus inhibition. When inhalation anesthesia followed this preoperative medication, there was usually less respiratory depression than that following either morphine or morphine and scopolamine. Certain added precautions, however, were found necessary during the immediate post-operative period if nembital was substituted for morphine. Patients under the influence of a barbiturate apparently perceive pain and misinterpret painful stimuli. For this reason, we believe, they become restless and excited. To prevent such occurrences, we have administered an opiate near the end of the operation, or at least before complete recovery from the anesthetic has taken place.

COMMENT

Nembital (sodium pentobarbital) is a popular sedative in use by both the medical profession and the lay public. That this drug has definite stimulative and depressant qualities is demonstrated by the above experiments. The addition of scopolamine lessens the depressing effects of nembital. This is particularly true with respect to minute volume exchange of air to and from the lungs. There is less depression of the respiratory functions with nembital than with morphine. The combination of nembital and scopolamine causes less respiratory depression than that caused by morphine and scopolamine. The addition of scopolamine to nembital provides a less profound, longer acting and more pleasant sedation than nembital alone in spite of the apparent greater restlessness. We believe that the combination of nembital and scopolamine is satisfactory for preoperative sedation and mucus inhibition, but that the combination cannot be depended upon to relieve pain.

REFERENCE

1. Wangeman, C. P., and Hawk, M. H.: *The Effects of Morphine, Atropine and Scopolamine on Human Subjects, Anesthesiology* 3: 24-36 (Jan.) 1942.