ANAESTHETIC DOSAGE IN THIOPENTAL-CURARE-NITROUS OXIDE ANAESTHESIA, USING A THIOPENTAL-CURARE MIXTURE

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THE advance presented by the introduction of short-acting barbiturates and muscle relaxants in anaesthesiology is recognized universally. However, the very ease with which patients are anaesthetized by this technique makes it more exacting for the anaesthetist than earlier methods.

Following unfortunate experiences with barbiturates and muscle relaxants in their early usage it was stated repeatedly that these drugs were dangerous when used in combination for lengthy procedures (1, 2). Another school of thought practised the restriction of barbiturates to the induction period, after which the patients were switched to some other anaesthetic for maintenance (3). Additional criticism was directed against the use of a thiopental-curare mixture (Baird's solution) (4) as it was thought to reduce the flexibility of the technique.

Contrary to these sentiments our impression is that properly managed barbiturate-curare-N₂O anaesthesia is among the better and safer anaesthetic techniques available today; and its administration is further facilitated by adoption of the thiopental-curare mixture in lieu of the separate agents.

In view of this divergence of opinion it appeared desirable to examine more closely the time-dosage relationship in thiopental-curare-N₂O anaesthesia and to compare it with data from the literature regarding the separate use of the same agents. It was hoped that the results would permit conclusions about the relative merits of the two techniques.

MATERIAL AND METHODS

This investigation comprises 86 cases lasting from 1 to 9 hours. One anaesthesiologist managed 71 cases; the remaining 15 were conducted by several others. The anaesthetic experience of these individuals varied considerably. In each case the time and amount of every dose of thiopental-curare was noted on the anaesthetic chart. A fixed concentration of 50 per cent nitrous oxide and 50 per cent oxygen was inhaled by all patients throughout the operations. The types of procedure, age of the patients, and anaesthetic utilization are presented in Table I.

The rate of anaesthetic utilization was determined for each patient according to the following formula:

$$R = \frac{\text{thiopental-curare mixture used (mg/kg)}}{\text{anaesthesia time}}$$

These rates were grouped into six classes according to length of anaesthesia. The average rates of utilization for each class were calculated. The standard error of the means was determined by the accepted formula (5):

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$$SE_M = \sqrt{\frac{N\sum x^2 - (\sum x)^2}{N^2(N-1)}}$$

The average totals of anaesthetic used in each class were determined by multiplying the average utilization rates by the midpoint anaesthesia times. The average intubation dose also was determined along with the average time that had elapsed from the administration of the intubation dosage to the administration of the next increment of thiopental-curare mixture. Although 78 patients in this series were intubated, data from only 49 cases were available for the latter determination.

TABLE I

<i>Type of operation</i>	1-2	2-3	3-4	4-5	5-6	6+	TOTAL
	HOURS ANAESTHESIA TIME						
Head and neck	2	3	4	—	—	—	9
Open chest	2	4	8	8	3	4	29
Intraperitoneal	3	5	9	9	4	3	33
Others	4	8	2	1	—	—	15
<i>Age groups</i>							
-2	1	—	1	—	—	—	2
2-15	2	2	2	2	1	—	9
15-60	8	12	15	11	3	6	55
60+	—	6	5	5	3	1	20
<i>Thiopental-curare mixture used (cc)*</i>							
-20	4	1	1	2	—	—	8
20-40	6	9	11	7	—	1	34
40-60	1	10	8	8	6	2	35
60+	—	—	3	1	1	4	9
TOTAL	11	20	23	18	7	7	86

*Each cc of thiopental-curare mixture contains 25 mg thiopental and 0.75 mg. d-tubocurare.

RESULTS

A representative example of individual time-dose curves is shown in Fig. 1.

The average utilization rates are plotted against the midpoints of the anaesthetic time classes in Fig. 2.

The averages of total utilization are plotted against the midpoints of the anaesthetic time classes in Fig. 3. An additional point is gained in this coordinate system by plotting the average intubation dosage against the average time after which the next increment became necessary.

THIOPENTAL
MG/KG

FIG. 1.

FIG. 1. Sample cumulative time-dose curve Patient intubated at 0 hr., awake and transferred to recovery room at X.

DISCUSSION

The most surprising feature revealed by the individual time-dose curves was that sudden variations in the degree of surgical stimulus, such as occur in the course of every operation, were not accompanied by large enough changes in drug requirements to distort the curvilinear relationship. Theoretically such behaviour would be explicable if the patients were carried at too deep a plane of anaesthesia all the time. By all clinical criteria available this was not the case.

The smoothness of the curve shown in Fig. 2 appears all the more remarkable because the number of observations is relatively small and the data were obtained under operating room conditions by several anaesthesiologists working with different surgical teams.

Fig. 3 represents the average dosage of thiopental-curare mixture in the course of an operation. This claim needs further justification, because all but one of the points on which the curve is based were derived from average total anaesthetic utilizations of individual cases. It might be argued that though the endpoints may fall along a curve, it does not follow that the individual curves themselves resemble the curve thus defined. The belief that little error if any was introduced through this assumption is based on inspection of the 86 individual time-dose curves. They all appear similar to Fig. 3 and to one another. It is strengthened

FIG. 2. Average utilization rates of thiopental-curare mixture, grouped into six classes according to the duration of anaesthesia. The vertical lines indicate the standard error of means.

further by the good fit of the point computed from the intubation dosages to the curve that is otherwise defined by total dosages.

It follows from the way in which the curve in Fig. 3 was constructed that it will indicate the cumulative dosages required to maintain, for a given time, that clinical level of anaesthesia which is prevalent during the major part of the procedure. The difference between the (extrapolated) induction dose and the actual intubation dose is explained by the observation that intubation ordinarily requires a deeper initial level of anaesthesia than induction without intubation.

The maintenance of a clear airway and adequate respiratory exchange are among the principal safeguards of thiopental-curare- N_2O anaesthesia. These objectives are facilitated best by intubation. The widespread reluctance to perform intubation has been based occasionally on the fear that it will "unnecessarily" increase the dosage of anaesthetics. Fig. 3 objectifies the clinical impression that in procedures lasting over 45 minutes intubation will not increase the total anaesthetic consumption in the average patient.

FIG. 3. Dosage of thiopental-curare mixture during the course of anaesthesia. The first class (49 cases) is the plot of the mean intubation dose vs. the average time that elapsed between its administration and the administration of the next increment. All other classes represent average total utilizations of thiopental-curare plotted against the class midpoint anaesthesia times. Vertical lines indicate standard errors of the means.

In all procedures respirations were vigorously assisted throughout. The assistance was of the same order that proved adequate in other investigations (6) to maintain normal or lower than normal alveolar CO_2 -levels. The effectiveness of relatively small amounts of thiopental-curare mixture probably was due primarily to this factor (7).

Using a similar anaesthetic technique but separate syringes of thiopental and curare, Dundee (7) arrived at 8.5 mg. thiopental per kg. body weight as the induction dose and 12.46 mg/kg as the 90-minute value. Our corresponding data were 8.6 and 12.3 mg/kg respectively.* The thiopental-curare ratios in Dundee's work were 31:1, 24:1, 29:1, and 16:1 at different points in the course of anaesthesia with varying degree of respiratory assistance. The thiopental-curare ratio in our mixture is 33:1. It thus appears that with thiopental-curare mixture satisfactory operative conditions can be achieved by using probably less but certainly

*In an article published since the completion of this study (Canad. Anaes. Soc. J. 2:41, 1955) C. F. Egan finds the average intubation dose of thiopental for infants 9 mg/kg with the use of Baird's solution. In view of the fact that weight for weight infants require more anaesthetic than adults this finding is in excellent agreement with the present data.

not more curare than when the two agents are used separately. The thiopental consumption is about equal.

It should be emphasized that the surgical teams in this series insisted on profound, practically apnoeic relaxation of all the patients. Even so it was a rare occurrence that the patients were not sufficiently awake at the end of the procedure to maintain their airway and obey simple commands. Some of those who were not responding could be induced to respond after the administration of an anticurare agent, indicating that on these occasions they were overcurarized to some degree even at this ratio. Comparison of data from two institutions, as was done in the preceding paragraph, is fraught with uncertainties because of the differences in an unknown number of conditions. However, the validity of the conclusions drawn here can be challenged only in the unlikely event that it is shown that Dundee's series consistently required greater relaxation than these cases.

As indicated in Figs. 1 and 3, the bulk of the mixture was given at a fast rate during induction. If the patient happens to react adversely to one of the pharmacologic agents, this is the period when accidents would be most likely to occur, provided the rest of the anaesthesia is not mismanaged. Following induction the balance of the thiopental-curare mixture is given in smaller increments at ever increasing time-intervals. During this period there is ample opportunity to detect and correct complications. Should they occur, alternative agents and methods may be considered. Otherwise the safest practice is to continue maintenance with thiopental-curare, for there seems to be no reason to consider the length of a procedure *per se* to be a contra-indication to the use of these agents

SUMMARY

- 1 Analysis of 86 cases in which a thiopental-curare mixture (Baird's solution) was used, and a comparison with data obtained by others who administered the drugs separately, indicate that use of the mixture does not result in an increase of the dosage of either agent
2. Time-dose curves are presented to show that a definite curvilinear relationship exists between drug-utilization and the duration of anaesthesia.
- 3 In cases lasting over 45 minutes intubation will not increase the anaesthetic consumption.

RÉSUMÉ

On a déterminé les besoins anesthésiques de 86 malades soumis à l'anesthésie au thiopental-curare (la solution de Baird). On a découvert qu'il existait une relation curviligne très nette entre l'utilisation de la drogue et le temps d'anesthésie. La comparaison des présents énoncés avec ceux d'autres chercheurs qui ont administré le thiopental et le curare séparément, mais selon la même technique, indique qu'on a conservé la flexibilité de la technique en employant le mélange standard et qu'on pourrait réaliser une certaine économie de curare. Les résultats montrent aussi que, dans les interventions d'une durée supérieure à 45 minutes, l'intubation n'accroît pas les besoins anesthésiques totaux du malade moyen.

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