Left Ventricular Dynamics of Trained Dogs 
Anesthetized with Methohexital

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The cardiac response to intravenous administration of the ultrashort-acting oxybarbiturate anesthetic, methohexital sodium, was studied in trained dogs. Heart rate increased immediately and gradually declined to the control value 60 minutes later. Stroke volume decreased immediately, reversed transiently, and decreased again, to return gradually to the control value at one hour. Peak aortic flow velocity and peak aortic flow acceleration paralleled the triphasic response of stroke volume. Cardiac output decreased initially, then increased to above the control value to a maximum at the time of maximum heart rate, then decreased again to below the control value by 30 minutes. From 30 minutes to 60 minutes cardiac output gradually returned to the control value. (Key words: Anesthetics, intravenous; methohexital; Heart: myocardial function.)

Nearly 20 years have passed since publication of the first reports of the ultrashort-acting oxybarbiturate anesthetic, methohexital sodium. Methohexital was claimed to be less toxic than thiobarbiturates, the only ultrashort-acting barbiturates available at that time. It has also been said that recovery from anesthesia occurs more rapidly after methohexital than after equivalent doses of thiobarbiturates such as thiopental, thio- 
butobarbital, thiomyalyl, or thialbarbital. The short duration of action of methohexital has been ascribed to its high lipid solubility and to its rapid rate of metabolism. Little information about the cardiovascular effects of methohexital is available. The data which have been published are often difficult to interpret because they have been obtained in animals already anesthetized with other agents, or, in man, because data sampling was intermittent. The objectives of the present investigation were to record on a continuous basis changes in heart rate, stroke volume, cardiac output, peak aortic flow velocity, and peak aortic flow acceleration following administration of methohexital to trained dogs in which appropriate sensing devices had been chronically implanted. The entire course of anesthesia with methohexital was observed, and methohexital was the only agent administered.

Methods and Materials

The experiments were performed in four adult mongrel dogs of either sex weighing between 29 and 32 kg. With the dog anesthetized with pentobarbital, 30 mg/kg, iv, under sterile conditions, a thoracotomy was performed through the fourth intercostal space. An electromagnetic flow sensor was implanted on the ascending aorta and an ECG lead was implanted on the left ventricular surface. A reference ECG lead was implanted subcutaneously on the chest wall. All leads were brought out at the back of the chest. A square-wave electromagnetic flowmeter (Zepeda Instruments, Seattle) that has an amplitude-frequency response which is 3 db down at 35 Hz was employed. The aortic flow acceleration was derived by electronic differentiating circuits with a frequency response of 50 Hz. Stroke volume was determined by electronically integrating the area under each aortic flow pulse. The ECG was used to trigger a reset circuit so that stroke volume was computed on a beat-by-beat basis. A heart rate meter (Capstan, Seattle) was employed to obtain heart rate by detecting and averaging R waves of the ECG. The ECG, heart rate, stroke volume, aortic flow velocity, and aortic flow acceleration
were displayed on a heated stylus oscillograph (Sanborn, Massachusetts) with a frequency response of 60 Hz.

Ten days or more were allowed for recovery from the surgical procedure before experiments were performed. The ultrashort-acting oxybarbiturate, methohexital sodium, was administered intravenously over periods of 140 seconds at an average dose of 5.4 mg/kg after control data were obtained in the awake state while the dog rested quietly on its side. No other drug was employed. Ten experiments were performed on four dogs. Two dogs were anesthetized twice and two dogs were anesthetized three times. Intervals of seven to ten days were maintained between experiments.

The results for heart rate, stroke volume, peak flow velocity, and peak flow acceleration are expressed as percentages of the control value which immediately preceded methohexital administration. Cardiac output was calculated by multiplying stroke volume by heart rate and is also expressed as percentage of control.

Results

Figure 1 presents the mean changes, expressed as percentages of control, for the five variables studied during the ten administrations of methohexital. The induction phase lasted 40-140 seconds and is illustrated on the left of the abscissa between the origin and the first discontinuity in the time scale. The middle time segment, illustrated by the 5-minute point, represents surgical anesthesia. At the end of the third time segment, 60 minutes after administration of methohexital, the dogs were awake and able to stand and walk.

Figure 1 shows that heart rate increased immediately when methohexital was administered and then gradually returned to the control level at one hour. The three indices of ventricular mechanical performance, i.e., stroke volume, peak aortic flow velocity, and peak aortic flow acceleration, decreased immediately and then recovered nearly to control levels at the time of maximum heart rate before decreasing again, gradually to return once more to control levels 60 minutes later. The net effect of heart rate and stroke volume on cardiac output was an initial decrease during the 5-15-second interval of the induction phase paralleling changes in stroke volume. The reduction in cardiac output occurred because stroke volume decreased more than heart rate increased. In the second interval, from 5-15 to 15-25 seconds, cardiac output more than doubled because stroke volume returned nearly to control and heart rate more than doubled. In the third interval of the induction phase, from 15-25 to 30-60 seconds, heart rate and stroke volume both decreased, causing cardiac output to return to just above the control value. Heart rate continued to decrease while stroke volume increased steadily toward control from 1 to 60 minutes. The net effect of these changes was a continued decline of cardiac output. By 10 minutes it had reached the control value, and it continued to decrease below this level, reaching a minimum at 30 minutes. Cardiac output then paralleled the course of stroke volume, returning to the control value at 60 minutes.

Figure 2 is an oscillograph record of an individual response to methohexital administration. It illustrates the changes shown as average values in figure 1.

Figure 3 is an expansion of the first minute of the record of methohexital administration shown at a slower chart speed in figure 2. Figure 3 shows the early triphasic response of stroke volume, peak aortic flow velocity, and peak aortic flow acceleration and the large increase of heart rate followed by partial return to control.

Discussion

Administration of methohexital to trained unanesthetized dogs caused an increase in heart rate. This is consistent with the increased heart rate observed in man when anesthesia is induced with methohexital. In contrast to the present observations using awake animals for control measurements, when methohexital was administered to dogs previously anesthetized with pentobarbital sodium there was no significant change in heart rate.

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§ Trade name Brevital, Eli Lilly and Company, Indianapolis. Chemical name 1-methyl-5-allyl-5 (1-methyl-2-pentenyl) barbituric acid, sodium salt.
The administration of methohexital to trained unanesthetized dogs caused a reduction in cardiac output, followed rapidly by a large increase during the first minute, then by a slower decrease to and below the control value, followed by return to control after one hour. In man, cardiac output has been reported to be increased following methohexital administration. However, cardiac output was measured intermittently in these studies in man and the times of determinations were not clearly stated. Thus, it is difficult to compare the response of man with that of the trained dog, although the immediate response of the dog was also to increase cardiac output. Attempts to compare the response of the trained dog with that of man are further complicated by the use in man of other drugs, including other anesthetic agents, by repeated administration of methohexital, and by surgical manipulation of the subjects while they were anesthetized. Although other attempts have been made to study the cardiovascular effects of methohexital in dogs, these effects were obscured in these studies because the dogs were already anesthetized with pentobarbital or thiopental—chloralose. In the studies of dogs previously anesthetized with other agents, there was no change in cardiac output when methohexital was administered. This is not surprising, because the effect of at least one other barbiturate, pentobarbital, is similar to that of methohexital. Pentobarbital administration also results in tachycardia and reduction of stroke volume, peak aortic flow velocity,
INDUCTION OF METHOHEXITAL ANESTHESIA
peak aortic flow acceleration, and left ventricular dP/dt when administered to the unanesthetized dogs.10-13

The triphasic response of stroke volume, peak aortic flow velocity, and peak aortic flow acceleration during induction with methohexitol may represent direct depression of ventricular mechanical performance with a transient superimposed "sympathetic burst."13 This is possible because the transient reversal of ventricular depression occurs at the same time as the maximum tachycardia. Ventricular function may also be decreased because of methohexitol-induced decrease of venous return. Methohexitol has been shown to cause peripheral vasodilation and to lower peripheral resistance.14 Peripheral venous pooling may reduce ventricular preload, resulting in reduced peak aortic flow acceleration.15,16

The present studies emphasize that meaningful data on cardiovascular responses to intravenous anesthetics can be obtained only if control observations are made in the awake state and only if changes in function are continuously monitored.

References