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ACUTE HYPERTENSION DURING INDUCTION OF ANAESTHESIA AND ENDOTRACHEAL INTUBATION IN NORMOTENSIVE MAN

BY

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SUMMARY

In twenty-two normotensive patients anaesthesia was induced with thiopentone, nitrous oxide and oxygen, suxamethonium, and endotracheal intubation. Laryngoscopy and insertion of an endotracheal tube were immediately followed by an average rise in mean arterial pressure of 25 mm Hg (SE 2.2, range 2–45). There was no significant difference in this response between groups premedicated with morphine and with amylobarbitone. There was no evidence that this effect caused lasting damage in normotensive patients. The possible cardiac or cerebral complications which might result in hypertensive patients are discussed.

The usual circulatory responses to laryngeal and tracheal stimulation in anaesthetized man are tachycardia and a rise in arterial pressure. These facts are derived from studies during different forms of inhalational anaesthesia (Reid and Brace, 1940; King, Harris and Griefenstein, 1950; Burstein, Lo Pinto and Newman, 1950; King et al., 1951; Takeshima, Noda and Higaki, 1964), and are interpreted as being the result of reflex sympathoadrenal stimulation. This interpretation is confirmed by a recent study in anaesthetized cats (Tomori and Widdicombe, 1969), in which mechanical stimulation of the respiratory tract was shown to cause increased nervous activity in cervical sympathetic efferent fibres.

Sympathoadrenal stimulation, with a sudden rise in blood pressure, may cause left ventricular failure (Masson, 1964), myocardial ischaemia (Editorial, 1969), and cerebral haemorrhage (Davidson, 1968); these complications are more likely in the presence of coronary or cerebral atheroma, or hypertension. Convulsions may be precipitated in the pre-eclamptic patient.

It is established that laryngotracheal stimulation can lead to sympathoadrenal stimulation. The frequency and degree of this response in normotensive patients are less certain. The purpose of the present study was to measure the cardiovascular response to laryngotracheal stimulation in healthy normotensive patients during a widely used method of induction of anaesthesia. Anaesthesia was induced with thiopentone, followed by suxamethonium and the passage of an endotracheal tube. The effects of premedication with barbiturate and with morphine are also demonstrated.

METHOD

Patients.

Twenty-two patients for elective minor gynaecological surgery were allocated alternately into Groups 1 and 2, premedicated with amylobarbitone and with morphine respectively. The criteria for admission to the study were: 15–60 years of age; ASA Class 1 (Dripps, Eckenhoff and Vandam, 1967); normotensive (resting blood pressure less than 140/90 mm Hg); no regular medication with hypnotics or sedatives.

Procedure.

Each patient was examined by the anaesthetist on the day before operation. During the consultation the patient rested on her bed. Blood pressure and pulse rate were measured on three occasions during a period of 30 minutes. Throughout the study the blood pressure was measured by auscultation with a mercury manometer. With the patient supine and her head resting on one or two pillows, the arterial pressure was recorded to the nearest 2 mm Hg, the systolic pressure

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(SP) at the first sounds and the diastolic pressure (DP) at the first definite change in sounds. Mean arterial pressure (MAP) was taken as

$$\frac{2\ DP+SP}{3}\left(=DP+\frac{SP-DP}{3}\right)$$

On the night preceding surgery, oral amylobarbitone was given according to body weight: 35–50 kg, 100 mg; 51–65 kg, 150 mg; 66–80 kg, 200 mg.

On the day of operation, premedication was given by intramuscular injection 30–90 minutes (mean 54, SE 2.8) before induction of anaesthesia, as follows:

Group 1: amylobarbitone 2.0 mg/kg (10 per cent solution) and atropine 0.6 mg.

Group 2: morphine 0.2 mg/kg and atropine 0.6 mg.

Subsequent management was identical for both groups.

When the patient was in the waiting-room outside the operating theatre, an intravenous infusion of 5 per cent dextrose was started in the right arm, and a blood pressure cuff was applied to the left arm. Measurements of pulse rate and blood pressure were made at 15, 10, and 5 minutes preceding induction of anaesthesia. Preoperative blood pressure measurements were made by one of the authors and subsequent measurements by an assistant anaesthetist.

In the operating theatre, plate electrodes for an electrocardiograph were attached to the right arm and left leg, and a continuous lead II trace recorded on paper during the study. Pulse rate and blood pressure were recorded every 30 seconds. Pulse rate was measured from the electrocardiogram and was counted during successive 30-second periods. Blood pressure measurements were spoken out and recorded on tape. The microphone of the tape recorder was secured in place beside the Heidbrink expiratory valve on the anaesthetic machine, in order to record the respiratory rate.

At time zero thiopentone (2.5 per cent solution) 6 mg/kg was injected during 15 seconds. Respiration was assisted, and then controlled by manual ventilation with a face mask at a rate of 20–24 b.p.m. A Boyle machine semiclosed circuit with carbon dioxide absorber was used, with fresh gas flows of nitrous oxide 3 l./min and oxygen 3 l./min. At 1 minute, suxamethonium 1.5 mg/kg was injected during 15 seconds, and intermittent positive pressure ventilation (IPPV) continued. At 3 minutes, a curved-blade laryngoscope was inserted and a cuffed oral endotracheal tube (8 or 9 mm) passed. A water-based jelly was used to lubricate the tube. The tube was passed by the same anaesthetist on all occasions, and was in place within 20 seconds of laryngoscopy, except in one patient when 35 seconds were required. The cuff was immediately inflated to provide an occlusive seal.

At the time of endotracheal intubation, capillary blood was taken from the big toe for P_{CO_2} measurement and analyzed by the micro-Astrup method.

After intubation, IPPV was continued at a rate of 20–24 b.p.m., and the time of the first sign of returning neuromuscular conduction noted. Thereafter halothane 0.5–1.0 per cent (Fluotec vaporizer outside circuit) was introduced in seventeen patients. Suxamethonium was used intermittently in five patients who were having therapeutic termination of pregnancy.

As small a volume of 5 per cent dextrose as possible (50–200 ml) was infused during the study. The drugs were injected into the intravenous drip.

RESULTS

Description of patients.

Table I presents the pre-operative data concerning the patients in Group 1, premedicated with amylobarbitone, and Group 2, premedicated with morphine. Paired *t*-tests show no significant difference between the two groups.

Cardiovascular response of all twenty-two patients.

Figure 1 and table II present the means of heart rate and blood pressure from all twenty-two patients. The minimum mean MAP (86 mm Hg) occurred at 1 minute following induction (table II). This was similar to the mean resting MAP the previous day (85 mm Hg). Between 1 and 4 minutes after induction there was a rise of 43 mm Hg. Between 3 and 4 minutes the rise of 25 mm Hg immediately followed laryngoscopy and endotracheal intubation. This rise of 25 mm Hg is highly significant ($t=3.40$, $P<0.01$). The

TABLE I

Pre-operative data (means ± standard error).

	Number of patients	Age (yr)	Height (cm)	Weight (kg)	BSA (m^2)	Resting heart rate (beats/min)	Resting blood pressure (mm Hg)		
							Systolic	Diastolic	Mean
Group 1	11	33 ± 2.6	163 ± 1.8	57 ± 3.4	1.61 ± 0.05	75 ± 2.2	113 ± 2.8	70 ± 2.5	83 ± 2.7
Group 2	11	40 ± 3.3	161 ± 2.2	62 ± 1.8	1.65 ± 0.25	75 + 4.3	119 ± 3.1	70 ± 2.5	86 ± 2.6

Group 1, amylobarbitone premedication. Group 2, morphine premedication.

greatest individual rises between 1 and 4 minutes were from 90/70 to 168/150 mm Hg and from 100/75 to 190/130 mm Hg.

The mean capillary Pco_2 (eighteen patients) at the time of intubation was 42.6 mm Hg (SE 1.08).

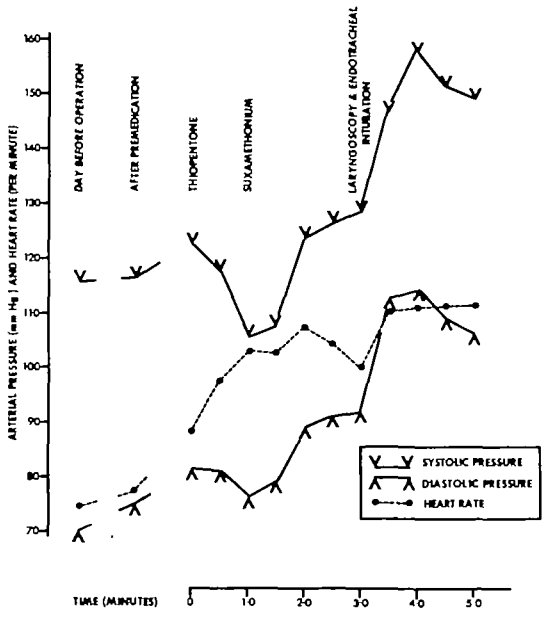

FIG. 1

Changes in mean systolic and diastolic pressure, and in mean heart rate, from twenty-two patients.

Electrocardiograph.

Three patients developed multiple extrasystoles, one during injection of thiopentone, and two within 2 minutes following endotracheal intubation. The e.c.g. changes in one patient were particularly interesting. During the 45 seconds following endotracheal intubation, the T-waves became flat, then inverted, and this was followed by multifocal ventricular extrasystoles. These changes were associated with a rise in blood pressure from 100/75 mm Hg at 1 minute after induction to 190/130 mm Hg at 4 minutes. Sinus rhythm then reappeared, and subsequent e.c.g. and clinical progress were normal.

Seven of the twenty-two patients developed cardiac slowing during laryngoscopy. In only one patient was the slowing greater than 10 per cent. On this occasion the pulse rate fell from 96 to 70 beats/min, but sinus tachycardia followed 20 seconds later. Sinus tachycardia followed endotracheal intubation in all patients (fig. 1).

Analysis of Groups 1 and 2.

Figures 2 and 3 compare the mean MAP and heart rate in the two groups of patients. To compare the effects of amylobarbitone and morphine premedication, analyses of variance were carried out on the blood pressure and heart rate data. In the latter case the treatment effect was significant ($t=2.45$, $P<0.05$), the heart rate being more rapid after morphine premedication. In the case of the blood pressure there was no significant difference.

At the time of intubation the mean Pco_2 (nine patients) in Group 1 was 43.9 mm Hg (SE 1.32). The mean Pco_2 (nine patients) in Group 2 was 41.2 mm Hg (SE 1.78). There was no significant difference between the groups.

Measurements at the end of the study.

The observations after 5 minutes are not plotted because of the return of neuromuscular conduction. The mean duration of action of suxamethonium was 5.1 minutes (SE 0.25).

The duration of hypertension cannot be stated exactly. There was a gradual return towards normal during the next 5–10 minutes. The maximum pressure in all patients occurred within 1 minute after intubation. At 4 minutes after

TABLE II

Means of heart rate and arterial pressure from twenty-two patients.

	Heart rate (beats/min) mean ± SE	Blood pressure (mm Hg) mean ± SE		
		Systolic	Diastolic	Mean (MAP)
Previous day	75 ± 2.4	116 ± 2.1	70 ± 1.7	85 ± 1.9
After premedication (min)	78 ± 3.1	117 ± 2.7	75 ± 1.8	89 ± 2.0
0	88 ± 3.8	123 ± 2.7	82 ± 2.4	95 ± 2.3
0.5	97 ± 3.8	118 ± 3.2	81 ± 3.2	93 ± 2.5
1.0	104 ± 3.6	107 ± 2.4	76 ± 2.2	86 ± 2.1
1.5	103 ± 3.1	108 ± 3.0	79 ± 2.9	89 ± 2.8
2.0	108 ± 2.7	124 ± 4.5	89 ± 3.6	101 ± 3.8
2.5	105 ± 3.1	127 ± 4.8	91 ± 3.8	103 ± 4.0
3.0	100 ± 3.1	129 ± 4.8	92 ± 3.5	104 ± 3.8
3.5	111 ± 2.8	147 ± 5.4	113 ± 4.1	124 ± 4.4
4.0	111 ± 3.0	158 ± 5.2	114 ± 2.8	129 ± 3.4
4.5	112 ± 3.1	152 ± 4.3	109 ± 3.3	123 ± 3.5
5.0	112 ± 3.5	150 ± 5.0	107 ± 3.0	121 ± 3.7

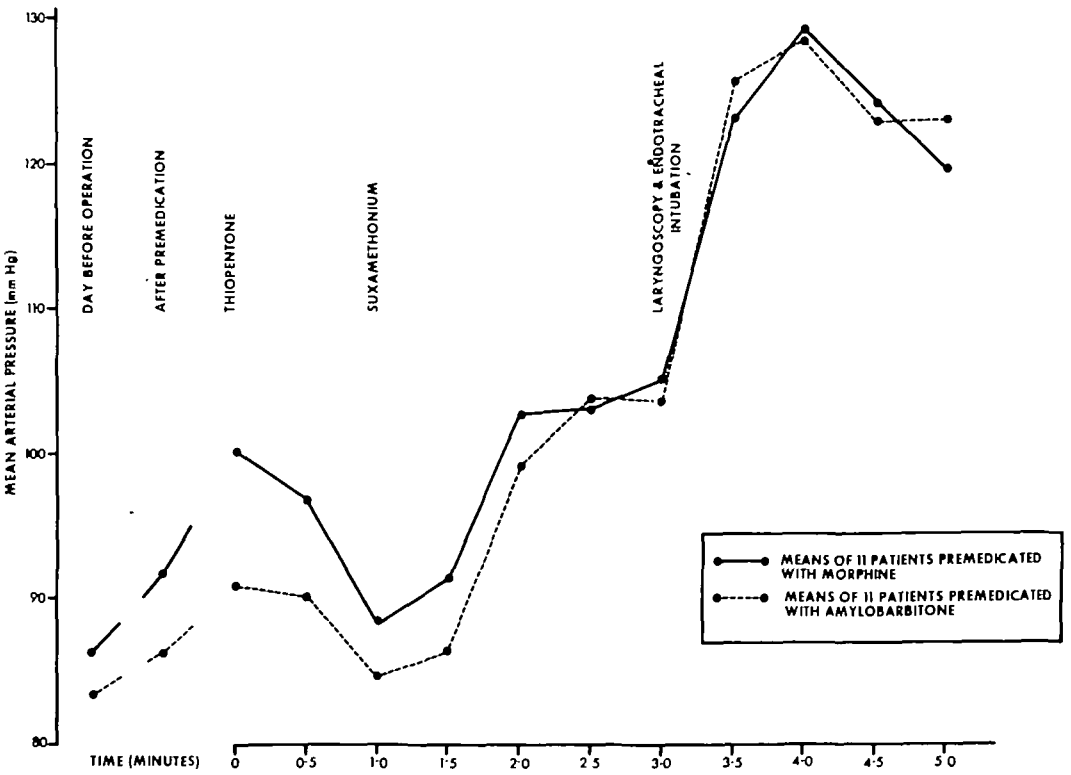

FIG. 2

Changes in mean arterial pressure during induction of anaesthesia.

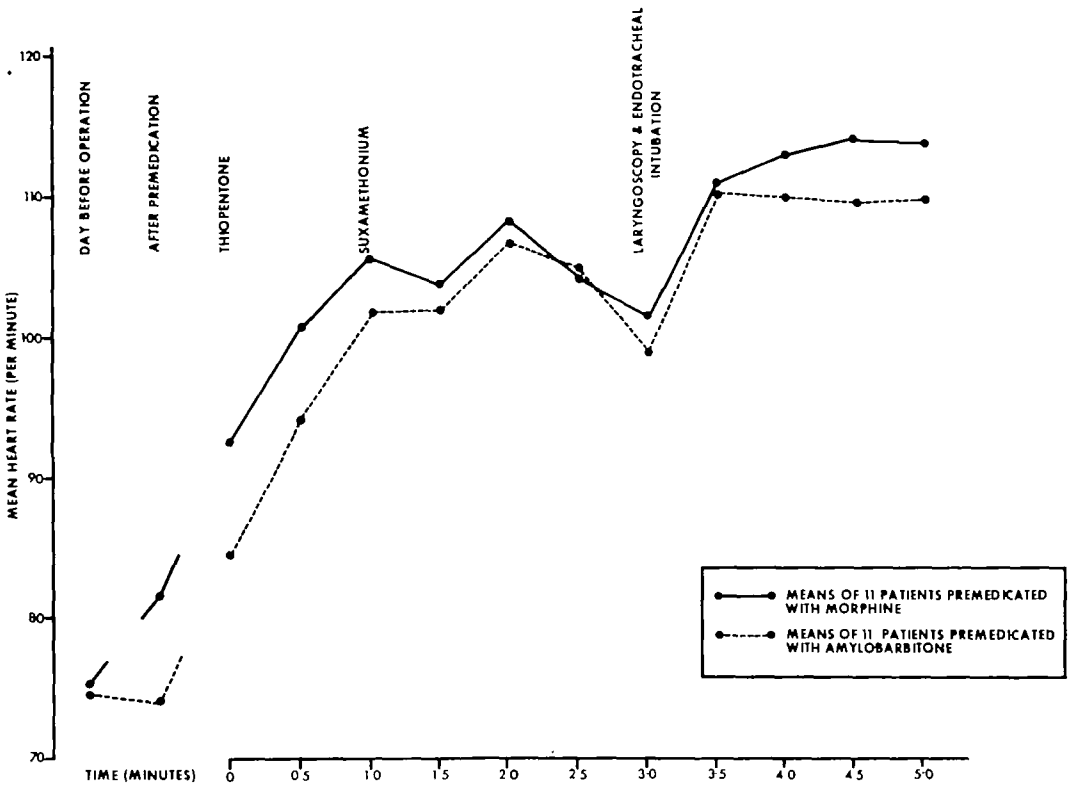

FIG. 3
Changes in heart rate during induction of anaesthesia.

intubation the mean MAP (fourteen patients) was 117 mm Hg (SE 3.83). Several patients coughed on the endotracheal tube at the end of the study and this was associated with either persistence of the raised blood pressure or a secondary rise.

DISCUSSION

During induction of anaesthesia with thiopentone, suxamethonium, and endotracheal intubation, normotensive patients showed a highly significant rise in mean arterial pressure (25 mm Hg, SE 2.2, range 2–45) within 1 minute of laryngotracheal stimulation. This can be explained on the basis of a reflex sympathetic response to mechanical stimulation of the larynx and trachea.

Other contributory causes of the hypertension, and tachycardia, could be continued manifestation of anxiety concerning anaesthesia and operation, atropine premedication, reflex baroreceptor effect consequent upon the fall in arterial pressure (9 mm Hg) after thiopentone, and a possible effect of suxamethonium (Takeshima, Noda and Higaki, 1964; Goodman and Gilman, 1967). These factors seem to be less important than laryngotracheal stimulation, particularly as the maximum rise in blood pressure immediately followed endotracheal intubation. Hypercarbia and hypoxaemia are other possible causes. The mean capillary Pco_2 at the time of endotracheal intubation was 42.6 mm Hg, and with an inspired oxygen concentration of 50 per cent and a fresh gas flow of 6 l./min, the arterial Po_2 must have been above normal. Hypercarbia and hypoxaemia can therefore be excluded as possible causes of hypertension.

The T-wave changes and ventricular extrasystoles observed in one patient could indicate myocardial ischaemia or strain. There was an associated rise in blood pressure from 100/74 to 190/130 mm Hg.

Premedication with intramuscular barbiturate and atropine is popular in the United States. Moreover, rapid induction of anaesthesia with thiopentone, suxamethonium, and endotracheal intubation is less favoured in the U.S.A. than elsewhere, because of the hypertension found in earlier studies with a variety of induction techniques (Reid and Brace, 1940; King, Harris and Griefenstein, 1950; Burstein, Lo Pinto and Newman, 1950; King et al., 1951). The authors examined the hypothesis that premedication with morphine and a moderately large dose of thiopentone (6 mg/kg) might produce a deeper level of anaesthesia at the time of endotracheal intubation, and therefore reduce any hypertensive reaction. However, from the viewpoint of minimizing changes in blood pressure, neither barbiturate nor morphine premedication gave any advantage.

The timing of drug administration and endotracheal intubation in this study was selected in order to approach as closely as possible a form of anaesthesia widely recommended for clinical anaesthesia (Wylie and Churchill-Davidson, 1966) and used during investigation of the cardiovascular response to other drugs (Tammisto and Welling, 1969). At the same time the intervals were such as to enable the maximum cardiovascular effects to be observed between each drug or stimulus.

Other studies.

In similar studies, Takeshima, Noda and Higaki (1964) found a mean rise in mean arterial pressure of 20 mm Hg at the time of laryngoscopy and intubation. They concluded that laryngoscopy was a more potent stimulus to hypertension than was endotracheal intubation. Some of these patients were hypertensive and the authors did not state the time interval between induction with thiopentone and endotracheal intubation. In nineteen hypertensive patients, who were being treated with hypotensive drugs, Dingle (1966) described a rise in mean arterial pressure of 34 mm Hg in response to endotracheal intubation.

Hypertensive patients.

Hypertensive patients have an exaggerated vasopressive response to many forms of stress, both in the conscious and in the anaesthetized state. From their clinical observations in hypertensive patients the authors have found that the rise of systolic pressure following endotracheal intubation may exceed 100 mm Hg. A rise in pressure of this order is potentially dangerous, and may lead to left ventricular failure and cerebral haemorrhage.

Moreover, just as sympathetic stimulation from any stress can provoke angina in the conscious patient, so during anaesthesia it may produce myocardial ischaemia. The mechanism of this may be that, with increased myocardial work and a demand for increased coronary flow, narrowed coronary arteries cannot accommodate the increased flow, and parts of the myocardium may receive insufficient oxygen (Editorial, 1969). This explanation may be one factor accounting for an appreciable mortality from myocardial infarction during the 24 hours following anaesthesia (Editorial, 1968).

Other complications are the rise in blood pressure and onset of eclamptic fits which have been observed to follow Caesarean section under general anaesthesia (Maternal and Perinatal Mortality Committee, 1969; Forbes, 1969, unpublished observations). This may also be associated with endotracheal stimulation, which could be as potent a cause of hypertension at the end of anaesthesia as at induction.

Clinical significance.

In this study of normotensive patients, a hypertensive response to laryngotracheal stimulation was present in all patients. The rise in blood pressure was significant, but the duration of hypertension was short-lived. With one exception there was no definite evidence of harmful effects, from the electrocardiogram or during the subsequent operative and postoperative period.

In hypertensive patients, on the other hand, the authors feel that there is a more compelling contraindication to this form of induction on account of an exaggerated hypertensive response. With all patients, but in particular those with cardiovascular disease, consideration should be given to the alternatives of deepening the level of anaesthesia with inhalational agents before endotracheal intubation (King, Harris and Griefenstein, 1951) or, when indicated, of using a regional technique such as epidural analgesia.

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HYPERTENSION AIGUE DURANT L'INDUCTION DE L'ANESTHESIE ET L'INTUBATION ENDOTRACHEALE CHEZ L'HOMME NORMOTENSIF

SOMMAIRE

Une anesthésie a été induite chez vingt-deux patients normotensifs au thiopentone, protoxyde d'azote et oxygène, avec suxamethonium et intubation endotrachéale. La laryngoscopie et l'insertion du tube endotrachéal ont immédiatement été suivies d'une augmentation moyenne de la pression artérielle moyenne de 25 mm Hg (ES 2,2, écarts 2–45). Il n'y eut dans cette réaction aucune différence significative entre les groupes avec prémédication de morphine et d'amylobarbitone. Il n'y eut pas d'évidence que cet effet serait de nature prolongée chez le patient normotensif. Les auteurs discutent les complications cardiaques ou cérébrales possibles, qui pourraient en résulter chez les patients hypertendus.

AKUTE HYPERTONIE WÄHREND DER NARKOSEEINLEITUNG UND ENDOTRACHEALER INTUBATION BEIM NORMOTENSIVEN MENSCHEN

ZUSAMMENFASSUNG

Bei zweiundzwanzig normotensiven Patienten wurde die Narkose mit Thiopenton, Lachgas und Sauerstoff sowie Suxamethonium eingeleitet und eine endotracheale Intubation vorgenommen. Unmittelbar auf die Laryngoskopie und Insertion eines endotrachealen Tubus erfolgte ein durchschnittlicher Anstieg des mittleren arteriellen Drucks von 25 mm Hg (SF 2,2; Streuung 2–45). Zwischen Gruppen, die als Prämedikation einmal Morphium und zum anderen Amylobarbiton erhalten hatten, wurde hinsichtlich dieser Reaktion kein signifikanter Unterschied festgestellt. Es ergaben sich keine Anzeichen dafür, daß dieser Effekt bei normotensiven Patienten einen Dauerschaden verursachte. Die möglichen kardialen oder zerebralen Komplikationen, die bei hypertensiven Patienten auftreten könnten, werden diskutiert.