SUDDEN DEATH DURING CYCLOPROPANE–ETHER ANESTHESIA FOLLOWING THE ADMINISTRATION OF EPINEPHRINE: CASE REPORT

MILTON H. ADELMAN, M.D.*

New York City

FATAL ventricular fibrillation during an inhalation anesthesia following the administration of epinephrine has been the subject of considerable experimental investigation.

Oliver and Schafer (1) demonstrated that ventricular fibrillation followed the injection of epinephrine into animals under chloroform anesthesia. This observation was confirmed and extended in the now classical studies of Levy (2). Meek, Hathaway, and Orth (3) have shown recently in dog experiments that cyclopropane has a marked "sensitizing" action on the cardiac automatic tissues, so that the administration of epinephrine was followed frequently by both ventricular tachycardia and ventricular fibrillation. These workers found chloroform to possess a sensitizing property less than that of cyclopropane, while ether showed less sensitization than chloroform. Meek (4) has presented recently a comprehensive review and critical analysis of the literature on the subject of cardiac automaticity and response to sympathomimetic drugs during inhalation anesthesia.

The literature shows a paucity of case reports of fatalities resulting from the administration of epinephrine in conjunction with an inhalation anesthesia. Guedel (5) has described two such fatalities under ether anesthesia. In one case, epinephrine had been used in a nasal pack before induction of ether anesthesia; sudden death occurred four to five minutes after induction. In the second case, sudden death followed the instillation of about ½ ounce of epinephrine in a frontal sinus of a patient under ether anesthesia. There have been no detailed reports of any such fatalities under cyclopropane anesthesia. Seevers and Waters (6) have mentioned the occurrence of a fatality under cyclopropane where death followed the accidental intravenous injection of epinephrine. Waters (7) has recorded without detail a death under cyclopropane and suggested that an intracardiac injection of epinephrine may have produced a fatal ventricular fibrillation. The purpose of this paper is to report a fatality under cyclopropane-ether anesthesia as a result of the injudicious use of epinephrine.

* From the Department of Anesthesia, Hospital for Joint Diseases, New York City.

CASE REPORT

Mrs. G. P., 34 years of age, was admitted with the complaint of urgency, frequency, and incontinence. Her family history was unimportant. Her past history revealed that she had had a cholecystectomy and appendectomy eight years before admission; also, one and one-half years before the present admission she had been hospitalized with complaints similar to those of her present illness, and had been discharged unchanged after a uterine curettage. Anesthesia in both operations was uneventful.

Physical examination revealed a moderately obese woman. The head and neck were found to be normal. The lungs were resonant to percussion; breath sounds were clear and vesicular. The heart was of normal size; the heart sounds were of good quality, regular sinus rhythm and free of any adventitious sounds. Blood pressure was 124/80. The abdomen was negative. Pelvic examination revealed a lacerated cervix and a cysto-rectocele.

Kahn and Kline tests were negative. Urine (uncatheterized) analysis showed a trace of albumin, many white cells and an occasional red cell. Blood hemoglobin was 13.2 Gm., erythrocytes totalled 4,660,000, and the leucocyte count was 7,400 with a normal differential.

On the day following admission the patient was brought to the operating room. The preliminary medication was morphine sulfate grain ¼ and atropine sulfate grain $\frac{1}{150}$, given hypodermically at 3 p.m. on going to the operating room. The anesthesia was administered by a nurse anesthetist and started at 3:25 p.m. The induction was performed with cyclopropane which was followed by ether. The induction was smooth and uneventful. During the induction the pulse was recorded at 72 per minute, respirations at 22 per minute and the blood pressure at 120/80.

The operation was begun at 3:37 p.m. with the patient in light surgical anesthesia. A dilatation and curettage was performed with the patient in lithotomy position. The condition of the patient was good. In preparation for a vaginal plastic operation, the surgeon then injected a total of 2 cc. of epinephrine (1:1000) into the four quadrants of the cervix; this was done in order to produce an avascular operative field. The anesthetist was not informed of this injection. An incision was then made into the vaginal mucosa overlying the cervix. At this point, about one minute after the administration of the epinephrine, the blood in the operative field was found to be very dark. At the same time the anesthetist observed sudden and profound cyanosis. The pulse was imperceptible and respiration ceased within a few seconds.

Artificial respiration was instituted immediately. Intravenous and intramuscular coramine was administered. An intracardiac injection of epinephrine was given. All efforts at resuscitation were of no avail and the patient was pronounced dead at 4:15 p.m.

Postmortem Examination (performed eighteen hours after death).

1. *Gross.*—The heart was somewhat dilated, the musculature soft and flabby. No subepicardial hemorrhages were noted. There was a small ecchymotic area surrounding a puncture wound on the anterior surface of the heart through which an intracardiac injection had previously been given. The coronary vessels were normal. The heart chambers were opened under water and no evidence of air embolism was found. The valves were normal in appearance. The aorta showed nothing unusual.

The lungs showed patchy bluish areas of atelectasis in all the lobes. They were moderately heavy and showed some evidence of pulmonary edema. On cross-section, fluid was easily expressed from the lung parenchyma. The bronchi and bronchioles were found to be normal in appearance. The pulmonary vessels were examined and no evidence of embolism could be found. There were no subpleural hemorrhages to suggest gradual asphyxia.

The gastro-intestinal tract was negative.

The liver was large and showed fatty changes.

The pancreas appeared edematous and congested.

The spleen was three to four times its normal size; the splenomegaly was due largely to intense hyperemia.

The kidneys and adrenals were normal.

The uterus showed no evidence of hemorrhage.

2. *Microscopic.*—The microscopic sections showed nothing remarkable, except as indicated in the anatomic diagnosis. There was nothing in the gross or microscopic findings to suggest asphyxia from anesthesia. Sections of the brain, except for congestion, showed nothing unusual.

3. *Anatomic Diagnosis.*

a. Status (fifteen minutes) after induction of anesthesia (cyclopropane-ether).
b. Status (several minutes) after dilatation and curettage and injection of adrenalin (2 cc. of 1:1000 solution) into the cervix in preparation for a vaginal plastic operation.
c. Dilatation of the heart.
d. Pulmonary edema.
e. Partial atelectasis of both lungs.
f. Hepatomegaly with fatty changes.
g. Obesity.

DISCUSSION

A review of the sequence of events in this case leads to the conclusion that the cause of death was ventricular fibrillation produced by epinephrine acting on a heart already sensitized by the inhalation agent.

One may pose the question as to which of the two inhalation agents used was responsible for the sensitization of the cardiac automatic tissues. The primary agent here was ether which will increase but slightly, if at all, the sensitivity of automatic tissues to epinephrine and other sympathomimetic amines. Indeed, Meek (4) has stated that "fibrillation may . . . occur in ether anesthesia from other causes but any relation to the anesthetic has not yet been demonstrated." The secondary agent employed was cyclopropane which was used for induction. Now, Meek and co-workers have shown the marked sensitizing effect of cyclopropane on the ventricular automatic tissues, an action even more marked than that of chloroform. Therefore, it appears that the cyclopropane, even though used for the brief period of induction, served to sensitize the heart, rather than the ether which was used to attain and maintain surgical anesthesia. Furthermore, analysis of the case justifies its classification as one of "cyclopropane-epinephrine syncope."

There still remains the possibility that this death was unrelated to the anesthesia and was caused by the epinephrine, per se. It is true that ventricular fibrillation can be produced in normal animals if enough epinephrine is used (4). Also, patients with heart disease are known to be predisposed to ventricular fibrillation following the administration of epinephrine (8). However, in this subject, young and in good health, it appears very unlikely that the epinephrine alone, in the dose used, was responsible for the death.

This case serves as a clinical counterpart and proof of the experimental work of Meek. It serves to emphasize the hazards of the use of epinephrine during inhalation anesthesia. It indicates the need for constant and unremitting vigilance by the anesthetist of the operative procedures and the therapeutic measures undertaken during an anesthesia.

SUMMARY

In a young healthy woman, under cyclopropane-ether anesthesia, the hypodermic administration of 2 cc. (1:1000) epinephrine (2 mg.) into the cervix uteri was followed by sudden death, probably due to ventricular fibrillation. The details of this case with postmortem findings are reported.

Analysis of the case justifies its classification as one of "cyclopropane-ether syncope."

REFERENCES

1. Oliver, G., and Schafer, E. A.: On the Physiological Action of Extracts of the Suprarenal Glands, J. Physiol. 18: 230, 1895.
2. Levy, A. G.: Sudden Death Under Light Chloroform Anesthesia, J. Physiol. 42: 3, 1911.
3. Meek, W. J.; Hathaway, H. R., and Orth, O. S.: The Effects of Ether, Chloroform and Cyclopropane on Cardiac Automaticity, J. Pharmacol. & Exper. Therap. 61: 240 (Nov.) 1937.
4. Meek, W. J.: Cardiac Automaticity and Response to Blood Pressure Raising Agents During Inhalation Anesthesia, Physiol. Rev. 2: 324–356 (April) 1941.
5. Guedel, A. E.: Inhalation Anesthesia, New York, Macmillan Company, 1937, p. 91.
6. Seevers, M. H., and Waters, R. M.: Pharmacology of the Anesthetic Gases, Physiol. Rev. 18: 447–479 (July) 1938.
7. Waters, R. M.: Present Status of Cyclopropane, Brit. M. J. 2: 1013 (Nov. 21) 1936.
8. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, Macmillan Company, 1941, p. 403.