EVIPAL FOR INDUCTION OF ANESTHESIA *

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THE intravenous administration of short-acting barbituric acid derivatives has become popular for induction of anesthesia and to complement other types of analgesia. Despite their deserved popularity, however, anesthesiologists have become cognizant of various complications that barbituric agents may produce. One type of complication that may be encountered is attributable to the result of increased respiratory vagal reflexes characterized by laryngeal spasm, bronchiolar constriction and coughing (1). These troublesome complications, in the human being, usually are unpredictable. Since pharmacologic observations have shown that these effects vary in different species and with different barbituric acid derivatives many barbituric acid compounds have been produced and assayed both in the laboratory animal and in the human being in an effort to find a drug with the least possible untoward side effects. One of the earlier barbituric acid derivatives used clinically is evipal. In a re-evaluation of this drug, its use in 10,000 cases during the last three years has been so satisfactory that the present report seemed justifiable.

Chemically, evipal is N-methyl-cyclo-hexenyl-methyl-barbituric acid. Its sodium salt, known as evipal sodium,† is a white powder that dissolves readily in water. It was first used clinically in 1933 and it gained popularity rapidly in the next few years. At that time, it was recommended to administer evipal intravenously in a 10 per cent solution. At present, it is deemed preferable to employ a more dilute concentration such as a 2 to 4 per cent solution. Other present safeguards used for other barbiturates are also recommended. These include preanesthetic medication with either atropine or scopolamine combined with a suitable opiate administered subcutaneously one hour previously. The desired effect following the intravenous injection of this barbiturate should not be to produce general anesthesia proper by it alone; rather, one should use this drug for its somniferous effect only and obtain analgesia in some other, safer manner. Finally, since there is some indication that this drug, like other barbiturates, may produce liver damage when given in *large* doses, it is recommended to limit its

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† The evipal sodium in this study was furnished by Winthrop-Stearns, Inc.

use for *induction* of anesthesia only. When used in this way, the desirability of evipal sodium soon becomes apparent.

TECHNIC

A 4 per cent solution of evipal sodium was found to be optimal. The contents of two ampules, each containing 1 gm., of evipal sodium are dissolved with 50 cc. of sterile distilled nonpyrogenic water in a glass, rubber stoppered bottle. This affords a stock solution which may be used repeatedly in the next forty-eight hours. The average amount of solution administered intravenously to produce induction of anesthesia in adults 16 to 60 years of age is 10 cc. (400 mg.). The rate of injection is fairly rapid, taking about one minute for 10 cc. Smaller appropriate doses may be given to younger patients 10 to 15 years of age and to adult debilitated patients. In patients between 60 and 70 years of age, caution should be used; if the preanesthetic medication has produced a satisfactory effect, evipal need not be used; if the patient is apprehensive, 5 cc. (200 mg.) may be injected intravenously slowly. Evipal is not used in patients over 70 years of age or in children under 10 years of age. (In the latter group, the children are given an hypnotic dose of a short-acting barbiturate rectally in their own room (2).) As soon as the patient loses consciousness, general anesthesia with nitrous oxide-oxygen or cyclopropane-oxygen is started.

Of particular interest is the fact that evipal sodium produces, in humans, less effects of respiratory vagal stimulation (laryngeal spasm, bronchiolar constriction and coughing) than pentothal sodium used in like manner. Volpitto and Benton (3) reported similar observations in their study of evipal sodium combined with *d*-tubocurarine for endotracheal intubation. The following case reports from our files are illustrative in this regard.

REPORT OF CASES

Case 1.—A 45 year old man sustained severe multiple injuries in an automobile accident. Numerous operations were required to treat his fractured pelvis, fractures of both legs, extensive burns, ruptured urethra and intestinal obstruction. His first 32 operations were performed with general anesthesia using sodium pentothal intravenously combined with nitrous oxide or cyclopropane. The patient liked the inductions with sodium pentothal and repeatedly requested that agent at his next session. However, each time that he lost consciousness following the intravenous administration of sodium pentothal he began to cough severely until a deep plane of inhalation anesthesia was attained; coughing was eliminated then but bronchiolar obstruction was persistent despite varied therapeutic measures such as administration of helium, positive intermittent breathing pressure and intravenous administration of atropine or isuprel. It was decided to use evipal sodium for his next operation to produce induction of anesthesia. The results were so gratifying that evipal induction was used for the remaining nine operations, with satisfaction on the

part of the anesthesiologist and of the patient. Coughing, laryngeal spasm and bronchiolar obstruction were not encountered in the last ten operations.

Case 2.—A 44 year old man had bilateral direct inguinal hernias. He was obese and gave a history of bronchial asthma. The surgeon decided to repair the hernia on one side at a time. The right inguinal hernioplasty was done on February 6, 1951. Preanesthetic medication consisted of morphine sulfate, 10 mg., combined with scopolamine hydrobromide, 0.4 mg., administered sucutaneously at 7:30 a.m. At the same time he was given 500 mg. of procaine amide by mouth in capsule form. Fifty minutes later anesthesia was induced by intravenous injection of 300 mg. of sodium pentothal in a 2 per cent solution. The patient began to cough violently as soon as consciousness was lost. Cyclopropane in oxygen by means of a closed carbon dioxide to-and-fro absorption technic was started immediately but the severe coughing continued. Despite the 60 per cent oxygen concentration being delivered to the breathing mixture, cyanosis developed and it became apparent that the patient had marked laryngeal spasm. The blood pressure rose sharply from 140 mm. systolic and 90 mm. diastolic to 210 mm. systolic and 120 mm. diastolic, while the pulse rate increased from 82 to 120 per minute. Manual pressure on the breathing bag was ineffective in overcoming the laryngeal barrier. Endotracheal intubation was quickly attempted and accomplished with difficulty owing to the persistent adduction of the true and false vocal cords. Compensated respirations by manual pressure on the breathing bag during the inspiratory phase partially improved the patient's condition. The respiratory pattern was that of bronchiolar constriction characterized by a short gasping inspiratory phase followed by a prolonged forceful expiratory phase. Auscultation of the chest corroborated this diagnosis by revealing loud râles during expiration. Addition of helium to the breathing mixture, injection of 0.6 mg. of atropine sulfate intravenously and the addition of ether to the breathing mixture did not overcome the bronchiolar constriction. Compensated respirations were maintained and since the circulatory status had improved, surgical intervention was allowed and completed in about one hour.

The postoperative course was surprisingly uneventful and the patient returned to the operating room one week later for hernioplasty of the other side. The same preanesthetic medication was administered and anesthesia was started by the same anesthetist at the same time interval after the premedication. Evipal sodium was used instead of sodium pentothal, 400 mg. of a 4 per cent solution being injected intravenously. The patient was asleep by the time the injection was completed (about 60 seconds). Respirations were maintained normally. There was no coughing. Cyclopropane anesthesia was immediately started in the same manner as previously. A pharyngeal airway was inserted, without reaction. Anesthesia was uneventful thereafter and the operation was completed without further complications.

Case 3.—A 54 year old man had multiple large tophi of gout on his feet, hands and elbows, which necessitated surgical excision. Induction of anesthesia by the intravenous injection of 300 mg. of sodium pentothal in a 2 per cent solution was followed by nitrous oxide-oxygen anesthesia and then by cyclopropane-oxygen. Two minutes after the injection of sodium pentothal, the patient had a bout of coughing which subsided as second plane inhalation anesthesia was attained. A "crowing" phonating noise at each inspiration then developed

and was maintained. Pulmonary ventilation seemed adequate but the "crowing" persisted during the entire procedure.

Two years later the patient returned for a similar operative procedure. Evipal sodium, 400 mg. in a 4 per cent solution, was used instead of sodium pentothal for induction of anesthesia. Anesthesia proper was again maintained by nitrous oxide at the beginning followed by cyclopropane. There were no respiratory or other complications.

There were at least 20 other patients in whom it was possible to compare the effects of induction of anesthesia by administering sodium pentothal at one time and evipal sodium at another time. In every instance in which sodium pentothal produced signs of respiratory vagal stimulation these signs were either absent or greatly diminished following the administration of evipal sodium.

In the entire series observed during the past three years, it cannot be claimed that the signs of respiratory vagal stimulation in question were never observed following the intravenous injection of evipal sodium. Coughing, laryngeal spasm, and bronchiolar constriction did occur at times, but the rarity of serious complications of this type was sufficiently convincing so that the use of evipal sodium was adopted as the barbiturate of choice to produce induction of anesthesia.

SUMMARY AND CONCLUSIONS

A re-evaluation on the use of evipal sodium for the induction of anesthesia has been made. Good results have been obtained by the intravenous injection of 10 cc. of a 4 per cent solution for the average adult patient.

The main advantage of this procedure is the marked decrease in quantity and in severity of signs of respiratory vagal stimulation characterized by coughing, laryngeal spasm and bronchiolar constriction ordinarily observed with other short-acting barbituric acid derivatives.

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AMERICAN BOARD OF ANESTHESIOLOGY

Written examinations of the American Board of Anesthesiology will be held in various locations, July 18, 1952. The oral examinations will be held in Swampscott, Massachusetts, September 28–October 1, 1952.