ELECTROCARDIOGRAPHIC STUDIES DURING ENDOTRACHEAL INTUBATION. V. EFFECTS DURING GENERAL ANESTHESIA AND HEXYLCAINE HYDROCHLORIDE TOPICAL SPRAY *

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IN previous communications it was found that the incidence of electrocardiographic disturbances *during* endotracheal intubation under general anesthesia could be reduced from over 60 per cent to about 17 per cent with procaine given intravenously and to 12 per cent with diethylaminoethanol or procaine amide, respectively, administered intravenously prior to intubation (1–4). During the course of these investigations it was noted that topical cocainization of the pharynx and larynx seemed to enhance cardiac disorders, producing especially ventricular premature contractions. In an effort to overcome this peculiarity of cocaine to sensitize cardiac automatic tissue through stimulation of the sympathetic nervous system while retaining the beneficial features of local anesthesia, other topical agents have been tried. Unfortunately, some of these are also toxic in their own right, stimulating the central nervous system or depressing circulation.

A new local anesthetic agent, "cyclaine®," has been under investigation for some time and seems to be associated with a low index of toxicity as well as good topical anesthetic properties (5, 6). Cyclaine is hexylcaine hydrochloride (1-cyclo hexyl amino 2-propyl benzoate hydrochloride), with a molecular weight of 297.85, and is freely soluble in water. A 1 per cent aqueous solution has a pH of 4.4 (unbuffered) and is stable under conditions of boiling and autoclaving. It has been used in spinal and regional anesthesia but has not been widely used as a topical anesthetic agent. Studies indicate that it possesses an order of toxicity comparable to that of procaine and neothesin, and an order of topical anesthesia comparable to that of cocaine and butacaine.

METHOD

Spraying the pharynx and larynx, including the epiglottis, vocal folds and rima glottidis but not the trachea proper, with approximately

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5 cc. of a 5 per cent aqueous solution of cyclaine after induction of general anesthesia forms the basis of this study. No instance of toxicity of the central nervous system or sympathetic nervous system was noted.

Control electrocardiograms of the first 3 standard leads were obtained in all patients before anesthesia was started. Subsequent lead II electrocardiographic tracings were taken (1) during light surgical anesthesia, (2) during exposure of the glottis and spraying, (3) at the moment of intubation, three to six minutes after spraying with cyclaine, and (4) three to five minutes after intubation. Tracings were made in 50 patients who were to undergo surgical intervention in whom endotracheal intubation was a desired procedure. Cases were not selected as to risk, disease or presence or absence of existing heart disease or arrhythmias. An attempt was made to intubate on the light side, that is, upper or middle second plane.

RESULTS

Cyclopropane-Ether Series.—In 20 patients, anesthetization was accomplished with cyclopropane and ether. Eleven of this number had regular sinus rhythm at the time of intubation or afterward. It is noteworthy that of these, in 2 cases a shifting pacemaker (fig. 1), in 3 cases a sinus bradycardia, in 2 cases a sinus tachycardia, and in one

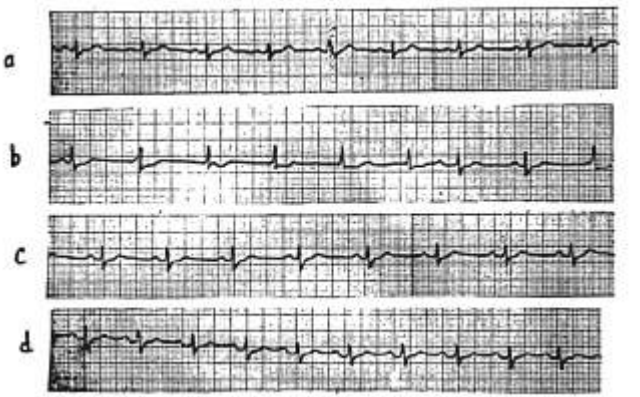

FIG. 1. Clearance of shifting pacemaker during cyclopropane-ether anesthesia following topical spray of larynx with 5 per cent cyclaine® solution. a. Control electrocardiogram, lead II showing regular sinus rhythm at a rate of 84 per minute. b. During second plane cyclopropane-ether anesthesia, the electrocardiogram shows a shifting pacemaker. The glottis and larynx were sprayed with 5 cc. of 5 per cent cyclaine immediately following this tracing. c. Two minutes after spraying with cyclaine, regular sinus rhythm, rate 75. Endotracheal intubation was accomplished during this tracing without change in the electrocardiogram. d. Two minutes later, regular sinus rhythm, rate 95.

case a regular sinus rhythm with nodal premature contractions (fig. 2) reverted to regular sinus rhythm *after* spraying with cyclaine, and the regular sinus rhythm was then maintained at the time of intubation. Similarly, in one case the control electrocardiogram, which was normal, was converted to a first degree heart block 3:2, with Wenckebach phenomenon and rare ventricular premature contractions. Following cyclaine spray, this reverted to regular sinus rhythm which was maintained during and after intubation (fig. 3).

In 7 cases, the only change seen at intubation was a sinus tachycardia, but in 3 of these, this rhythm existed before induction.

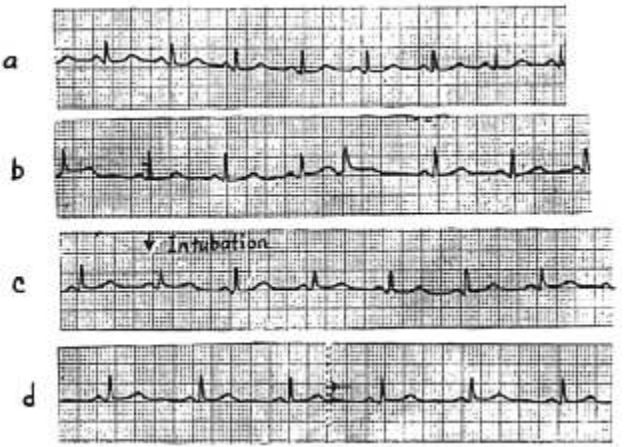

FIG. 2. Clearance of nodal premature contractions during cyclopropane-ether anesthesia following topical spray of larynx with 5 per cent cyclaine® solution. a. Control electrocardiogram, lead II showing regular sinus rhythm at a rate of 90 per minute. b. During second plane cyclopropane-ether anesthesia, the electrocardiogram shows nodal premature contractions. The glottis and larynx were sprayed with 5 cc. of 5 per cent cyclaine immediately following this tracing. c. Four minutes later, before and during endotracheal intubation, the tracing shows a regular sinus rhythm. d. Three minutes after intubation, no change.

In one case, a regular sinus rhythm was maintained at the time of intubation but a bigeminal auricular premature contraction developed afterward.

In one case, a first degree heart block was converted into a complete heart block at the time of intubation.

This leaves 14 of 20 cases which showed no change from the basic rhythm and 4 additional cases with only the development of sinus tachycardia, not usually considered an ominous arrhythmia.

Cyclopropane Series.—Anesthetization was carried out with cyclopropane alone in 11 patients.

Five patients showed no change from a regular sinus rhythm at the time of spraying, during intubation or afterward.

In 5 patients sinus tachycardia developed *after* intubation when anesthesia was lightening; during the passage of the endotracheal tube no change was observed. Furthermore, 2 of these 5 patients already had a preinduction sinus tachycardia and another had an abnormal electrocardiogram with nonspecific ST and T wave changes.

In only one patient in the cyclopropane series was any type of serious arrhythmia demonstrated. It is to be noted that in this patient

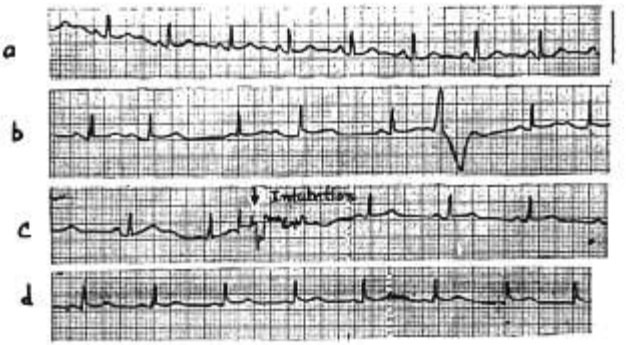

FIG. 3. Clearance of first degree heart block with ventricular premature contractions during cyclopropane-ether anesthesia following topical spray of larynx with 5 per cent cyclaine®. a. Control electrocardiogram, lead II showing regular sinus rhythm. b. During second plane cyclopropane-ether anesthesia, the electrocardiogram shows a first degree heart block, 3:2, with Wenckebach phenomenon and rare ventricular premature contractions. The larynx was then sprayed with cyclaine. c. Three minutes after spraying with cyclaine, before and during endotracheal intubation, the tracing shows a regular sinus rhythm at a rate of 65 per minute. d. Five minutes after intubation, no change.

an obstruction was present after spraying and the first attempt at intubation resulted in failure. Bigeminal ventricular premature contractions developed *before* intubation but were converted to a sinus tachycardia on intubation and reverted to regular sinus rhythm three minutes afterward (fig. 4).

The remaining 19 patients in this study were anesthetized with various other combinations of agents, including pentothal and cyclopropane, pentothal and curare, pentothal and cyclopropane-ether, nitrous oxide and ether, pentothal and nitrous oxide, evipal and nitrous oxide-ether. One patient, while awake, was intubated with 5 per cent cyclaine topical anesthesia only and then anesthesia was induced with cyclopropane and ether.

Fourteen cases showed no change from their basic rhythm. Nine patients with regular sinus rhythm showed no change from regular sinus rhythm. Five of these had sinus tachycardia before induction and this rhythm was maintained during intubation, the rate increasing slightly in three to five minutes.

Of the 5 patients who had changes in rhythm, 2 patients with regular sinus rhythm had sinus tachycardia after intubation. First degree heart block with Wenckebach phenomenon developed in one patient who had sinus tachycardia and a PR interval of 0.2 second. One patient with hypertensive arteriosclerotic heart disease and a history of myocardial infarction had rare nodal premature contractions three minutes after intubation. In one patient with right bundle branch block

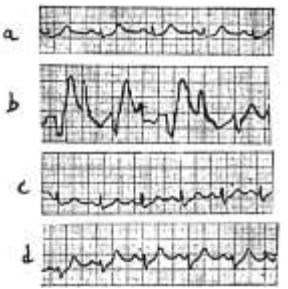

FIG. 4. Clearance of bidirectional ventricular premature contractions during cyclopropane anesthesia with obstruction following topical spray of larynx with 5 per cent cyclaine®. a. Control electrocardiogram, lead II showing normal regular sinus rhythm. b. During second plane cyclopropane anesthesia with respiratory obstruction, the electrocardiogram shows bidirectional premature ventricular contractions. The larynx had just been sprayed with 5 cc. of 5 per cent cyclaine. c. Two minutes later, during endotracheal intubation, the tracing shows a sinus tachycardia, rate 120 per minute. d. Three minutes later, no change.

there was no change during intubation while awake, after topical administration of 5 per cent cyclaine, but slight hypoxia was experienced when anesthesia was induced with cyclopropane and ether, and transient, bigeminal, ventricular, premature contractions developed.

COMMENT

Means generally employed to abolish arrhythmias during intubation include deepening the plane of anesthesia, or adding such cardiac depressors as quinidine, procaine or procaine derivatives, or a combination of both. Some investigators have tried to protect the patient by intravenous administration of barbiturates. Unfortunately, either pulmonary ventilation is depressed, often to such a degree as to bring in the factors of oxygen lack and carbon dioxide retention, or the addi-

tion of depressants produces undesired changes. To obviate these disturbing features an attempt was made to approach the problem by removing the afferent arc of the reflex by which it is thought such arrhythmias are produced. Cocaine, although an efficient topical agent for this purpose, may in itself be toxic to the cardiovascular system. Previous observations have shown that not only circulatory depression and collapse but serious arrhythmias may result when cocaine is used in this connection. Preliminary studies have shown that 5 per cent aqueous solution of cyclaine possesses adequate topical anesthetic properties for the larynx (7). In our experience this is confirmed and is associated with a low order of toxicity. Furthermore, cyclaine is unique in that it apparently has qualities similar to those of procaine in its anti-arrhythmic effects. This is well illustrated in the accompanying illustrations (fig. 1 to 4). The comparative incidence of arrhythmias when cocaine was utilized in other series was not significantly diminished when compared with the incidence following intubation without topical anesthetization. For example, in one group of 40 cases, various abnormal cardiac rhythms were noted in 31. By contrast, when cyclaine was used, the over-all incidence of arrhythmias was 30 per cent, and the actual incidence during intubation was 14 per cent.

SUMMARY

Electrocardiographic tracings were obtained in 50 adult patients who were given general anesthesia complemented by topical anesthetization of the pharynx and larynx with a 5 per cent aqueous solution of cyclaine. Electrocardiographic disturbances occurred in 14 per cent of the cases at the time of intubation. This incidence compares favorably with that in the previous series, including those in which procaine, diethylaminoethanol and procaine amide were used prior to endotracheal intubation. In the series in which procaine or its derivatives had been omitted under similar conditions the incidence of such disturbances was more than 60 per cent. Past experience has not helped to reduce the frequency or severity of these arrhythmias by using cocaine as a topical anesthetic agent. Cyclaine, a clinically new local anesthetic agent with adequate topical anesthetic properties, has been found to be free from sensitizing effects and, in addition, to possess a procaine-like action in actually clearing some arrhythmias produced.

ACKNOWLEDGMENT

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Thursday, April 9, 1953

Pharmacology of Autonomic Blocking Agents—Mark Nickerson, Ph.D., M.D., Associate Professor of Pharmacology, University of Michigan School of Medicine, Ann Arbor.

Reflex Changes During Anesthesia—E. M. Papper, M.D., Executive Officer of the Department of Anesthesiology, College of Physicians and Surgeons, Columbia University; Director of the Service of Anesthesiology at the Presbyterian Hospital, New York, N. Y.

Management of Anesthesia Associated with the Autonomic Nervous System—Harvey Slocum, M.D., Professor and Chairman, Department of Anesthesiology, University of Texas, Medical Branch, Galveston.

Commissurotomy: The Effects of the Autonomic Nervous System and Their Management—Harold Miller, M.D.

Newer Sympathomimetic and Parasympathomimetic Agents—Mark Nickerson, Ph.D., M.D.

Nerve Injuries Incident to Anesthesia—Morris J. Nicholson, M.D., Department of Anesthesiology, Lahey Clinic, Boston.

Diagnostic and Therapeutic Uses of Regional Anesthesia—Frederick P. Haugen, M.D., Associate Professor of Surgery, Head of Division of Anesthesiology, University of Oregon Medical School Hospitals and Clinics, Portland, Oregon.

Round Table—Diagnostic and Therapeutic Uses of Regional Anesthesia.

E. M. Papper, M.D.—Moderator
Frederick P. Haugen, M.D.
John J. Bonica, M.D.
Daniel C. Moore, M.D.
J. Samuel Denson, M.D.
Horace B. Graves, M.D.

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