THE SYMPATHOMIMETIC EFFECT OF COCAINE IN THE PRODUCTION OF CARDIAC ARRHYTHMIAS DURING CYCLOPROANE ANESTHESIA* †

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The fact that anesthetics, particularly cyclopropane and chloroform, sensitize the automatic tissues of the heart to epinephrine and related adrenergic drugs has been known for some time. Numerous reports of studies made during the combined use of various adrenergic drugs and cyclopropane or chloroform are available. Because of its local vasoconstrictor action, its ability to dilate the pupil, and its systemic pressor effect, cocaine is referred to as sympathomimetic. Certain writers (1, 2) have indicated that cocaine may increase cardiac irritability particularly if used with cyclopropane and other anesthetics which sensitize the heart. Since it frequently is used as a topical anesthetic for endotracheal intubation in conjunction with cyclopropane, it is important to establish without question whether or not it enhances cardiac irritability. We believed from extensive clinical use that this contention is not correct, but we had no concrete data to support our impression. This study was undertaken to shed some light on this question.

Ruben and Morris (3) administered cocaine and epinephrine intravenously to dogs anesthetized with cyclopropane. Cocaine alone did not cause arrhythmias. However, evidence that cocaine enhanced the action of epinephrine in causing arrhythmias was obtained. Naturally, it would be impossible to repeat this study on man. However, we have obtained data shedding light on this subject, by using cyclopropane and cocaine together for endotracheal intubation.

METHOD

All types of patients were used in this study. Patients with cardiac disease were excluded, however. The patients were deeply anesthetized with cyclopropane, given 20 mg. of succinylcholine intravenously in one dose to facilitate intubation and intubated orally by direct laryngoscopy. After the intubation, 2 ml. of 4 per cent cocaine or 5 per cent hexylcaine was instilled into the trachea through the endotracheal catheter. Electrocardiographic tracings (lead II) were taken throughout induction and for 10 minutes after intubation.

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TABLE 1

RESULTS

<table>
<thead>
<tr>
<th>Total cases</th>
<th>27</th>
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<tr>
<td>Arrhythmias following cocaine</td>
<td>7 or 26%</td>
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Time of onset

Less than 30 sec.:
- Case 1 — 15 sec. 1
- Case 3 — 1 sec. 1
- Case 6 — Immediately 1
- Case 18 — 2 sec. 1

Total 4

More than 30 sec.:
- Case 4 — 2 min. 1
- Case 7 — 2½ min. 1 (during packing)
- Case 9 — 2½ min. 1 (during packing)

Total 3

Observations were made on 27 patients receiving cyclopropane and cocaine and 12 receiving cyclopropane and hexylcaine. Arrhythmias were placed in 2 categories: (a) those occurring within 30 seconds after intratracheal instillation of the drug and (b) those appearing after a lapse of 30 or more seconds. Arrhythmias occurring immediately after instillation of cocaine, we feel, are due to mechanical stimulation in the trachea and those occurring later to the systemic effect of the drug. If a mechanical reflex action causes the irregularities rather than a sympathomimetic action, agents devoid of sympathomimetic action should also cause arrhythmias under similar circumstances. To determine this, a parallel study using 5 per cent hexylcaine hydrochloride (cyclaine®) instead of 4 per cent cocaine was undertaken. Hexylcaine lacks the supposed sympathomimetic activity of cocaine.

Of the 27 patients studied, 7 or 26 per cent developed some type of

TABLE 2

TYPES OF ARRHYTHMIAS

Type
- Case 1 — Bigeminy
- Case 3 — Sinus arrhythmia
- Case 4 — Nodal rhythm
- Case 6 — Bigeminy
- Case 7 — Bigeminy
- Case 9 — Ventricular premature beats
- Case 18 — Bigeminy

Total 7 Cases

Case 20 — developed bigeminy during intubation which was relieved by cocaine

Case 27 — developed bigeminy during induction (Stage III, Plane I) which cleared only by intratracheal cocaine
irregularity after instillation of cocaine. Four of these occurred promptly, in less than 30 seconds. Three occurred after 30 seconds (table 1). The second patient of the series in which hexylcaine was used developed arrhythmias immediately following the injection of the drug. This appears to corroborate the feeling that irregularities which arise immediately after instillation of cocaine are of reflex rather than pharmacologic origin. Two patients (table 2) developed arrhythmias after intubation prior to the administration of cocaine which persisted despite therapy instituted to eliminate them. Hyperventilation with oxygen, the addition of ether, or deepening of anesthesia failed to restore regular rhythm. On both occasions, the arrhythmia disappeared promptly after the instillation of cocaine into the trachea. In a number of others, arrhythmias developed prior to intubation but did not persist.

**Discussion**

The arrhythmias occurring within 30 seconds after the administration of cocaine (table 1) occurred as soon as the drug came into contact with the trachea. Those appearing after 30 seconds following the instillation of cocaine occurred so long after the instillation that reflex arrhythmia may be discounted. This supports the belief that most of the arrhythmias which occurred in this series were initiated reflexly and were not due to the pharmacologic action of the cocaine. The appearance of arrhythmias after instillation of hexylcaine also substantiates this contention. Arrhythmias which could be ascribed to the action of cocaine occurred in 3 of the 27 instances. This, an incidence of 11 per cent, in our opinion, is too low to be significant.

The incidence of arrhythmias with cocaine (immediate or delayed) was far lower than the incidence encountered in the series of 100 cases using all techniques and agents (26 versus 56 per cent) (4). The types of arrhythmia noted are similar to those observed during cyclopropane anesthesia without cocaine. It is noteworthy that the types of arrhythmias observed using cocaine and cyclopropane are similar to those observed during endotracheal intubation in which ether is used alone or with cocaine or in cases in which there is no question of sympathomimetic activity (4). The arrhythmias caused by cyclopropane combined with epinephrine are usually ventricular in origin, such as ventricular tachycardia, nodal rhythm, and so on. They differ in many respects from the arrhythmias noted in this particular study.

No doubt larger quantities of cocaine and deeper and longer periods of cyclopropane anesthesia could cause disturbances characteristic of sensitization by an adrenergic drug. We did not feel justified in subjecting patients to the hazard involved to obtain these data.

**Summary**

Cocaine possesses certain pharmacologic effects which suggest it is a sympathomimetic drug. It has been suggested that the combina-
tion of cocaine and drugs which increase cardiac irritability may cause serious arrhythmias.

Electrocardiographic studies were made in surgical patients using the combination of cyclopropane and cocaine topically for intubation. A comparison was made between patients not receiving the combination and those receiving hexylcaine for topical anesthesia. The data indicate no difference between the drugs. The arrhythmias are no more frequent with the combinations than without. The arrhythmias are not of the type noted when epinephrine and cyclopropane are combined.

REFERENCES