COMPATIBILITY OF A SYNTHETIC OXYTOCIN (SYNTOCINON) WITH ANESTHESIA IN DOGS

STANLEY A. FELDMAN, M.B., DEAN M. FORGAARD, B.S.
LUCIEN E. MORRIS, M.D.

THE RECENT establishment of the structural formula of the oxytocic principle of the posterior pituitary (1) and its subsequent synthesis (2, 3) has allowed a chemically pure oxytocic, Syntocinon, to be introduced in obstetric practice. This has reopened the question of the compatibility of this type of drug with anesthetic agents. Cardiac collapse and death have been reported following the administration of posterior pituitary extracts to anesthetized patients (4, 5). Parsloe, Morris and Orth (4) studied the effects of various pituitary fractions on dogs during the administration of several anesthetics. Their findings correlated with subsequent clinical observations (6). These studies confirmed that Pitocin had little effect on the cardiovascular system. Since Syntocinon is credited with similar pharmacological effects to those of Pitocin (7), it is desirable to know whether this drug is equally safe to use with anesthetics.

An investigation has therefore been made of the effects of administering Syntocinon to dogs during cyclopropane anesthesia. The study was extended to include trichlorethylene and barbiturate anesthesia, since these agents are also commonly used in obstetrics.

METHOD

The study was conducted in the manner used by Parsloe, Morris and Orth (4) in their parallel research into the compatibility of various anesthetic agents with extracts of the posterior pituitary gland.

Observations were made of the effect of Syntocinon in a dose of one unit/kg. upon (a) cardiac conduction and blood pressure during cyclopropane, trichlorethylene and barbiturate anesthesia in dogs, and (b) the incidence and severity of epinephrine induced cardiac arrhythmias in dogs anesthetized with cyclopropane or trichlorethylene.

Dogs were anesthetized with cyclopropane, trichlorethylene or a barbiturate. The femoral artery was catheterized and connected to a Statham transducer for continuous monitoring of the blood pressure, the femoral vein was catheterized to facilitate intravenous injections and a lead 2 electrocardiogram was recorded. When the dogs had been maintained in surgical anesthesia for forty-five minutes a test dose of epinephrine, diluted to 5 cc. with saline, was injected intravenously at a

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uniform rate during an interval of fifty seconds, and the dose of epinephrine which would cause a short burst of ventricular tachycardia was ascertained for each animal, in the manner described by Meek, Hathaway and Orth (8). The effect of this challenge dose of epinephrine was subsequently studied at ten minute intervals after the administration of Syntocinon. Alterations in the irritability of the myocardium due to Syntocinon were reflected in changes in the duration and severity of the cardiac conduction abnormalities elicited. At least ten minutes were allowed to elapse between the test dose of epinephrine and the administration of Syntocinon, to ensure that the effects recorded were not influenced by the epinephrine. Care was taken to avoid any accumulation of carbon dioxide since it has been shown to depress the development of epinephrine induced arrhythmias (9, 10).

In the trichlorethylene studies anesthesia was induced with either sodium thiopental, succinylcholine or cyclopropane, to facilitate tracheal intubation and the dogs were then maintained on trichlorethylene and oxygen in a nonrebreathing system for forty-five minutes before being given Syntocinon. The results were comparable in all these cases, and it was therefore considered that barbiturate induction did not influence subsequent epinephrine induced arrhythmias, an observation similar to that made by Orth, Wangeman and Meek (12) with regard to cyclopropane. It was confirmed that under trichlorethylene anesthesia, the myocardium was extremely sensitive to epinephrine (13, 14).

Results

Syntocinon and Cyclopropane Anesthesia.—In 15 experiments on 8 dogs, Syntocinon was administered during cyclopropane anesthesia. The only observed abnormality of the electrocardiogram pattern was an occasional sinus bradycardia. In eight of these experiments a decrease in the mean blood pressure of from 10 to 40 mm. of mercury was noted, maximal at 1½ to 2 minutes and returning to normal in 3 to 4 minutes. In some instances these changes were preceded by a transient slight elevation of the blood pressure. A slight rise in the mean blood pressure of between 10 and 25 mm. of mercury was observed twice. When this occurred it persisted for 3 to 4 minutes and in one instance was associated with bradycardia. In the remaining five experiments no significant alteration of blood pressure was recorded.

Syntocinon and Barbiturate Anesthesia.—In three experiments Syntocinon was administered to dogs anesthetized with barbiturates, two with sodium thiopental and one with pentobarbital. In two of these dogs (one with sodium thiopental and one with pentobarbital) there was a slight rise in blood pressure. In the third dog no alteration was noted. The electrocardiogram remained normal throughout these experiments.

TABLE 1

EFFECT OF SYNTOCINON ON BLOOD PRESSURE UNDER ANESTHESIA

Anesthetic	Number of Experiments	No Effect	Rise in Blood Pressure	Fall in Blood Pressure
Cyclopropane	15	5	2	8
Trichlorethylene	3	0	3	0
Barbiturates	3	1	2	0

Syntocinon and Trichlorethylene.—Syntocinon was given to three dogs anesthetized with trichlorethylene. A rise in the mean blood pressure of 10 to 35 mm. of mercury was recorded in each. One dog showed bradycardia and exaggerated sinus arrhythmias, coinciding with the elevated blood pressure. Comparison of these effects is shown in table 1.

Effect of Syntocinon on Epinephrine Induced Arrhythmias.—Twelve experiments were performed on seven dogs maintained in surgical anesthesia with cyclopropane. In two experiments when Syntocinon was administered together with epinephrine the duration and severity of the arrhythmias elicited were comparable to those obtained with the standard dose of epinephrine alone. When the individual challenge dose of epinephrine was given 10 minutes after the Syntocinon, it failed

TABLE 2

EFFECT OF SYNTOCINON ON EPINEPHRINE INDUCED ARRHYTHMIAS DURING CYCLOPROPANE ANESTHESIA

Dog	Duration of V.T. with Control Epinephrine	Occurrence and Duration of Ventricular Tachycardia in Secs., After Syntocinon Administration							
		After 10 Minutes	After 20 Minutes	After 30 Minutes	After 40 Minutes	After 50 Mintues	After 60 Minutes	After 75 Minutes	After 90 Minutes
A	12	+	32						
A	5	+	12	V.F.					
B	55	32	36	48					
B	58	18	25		30	65			
C	55	22	35	64					
‡D	40	+	+	+	5	+	0	0	0
E	45	+	5	35	38	50			
E	57	27	35	38	50				
F	18	8	+		+	3	5	+	15
G	7	2	+	+	+			3	
During Trichlorethylene Anesthesia									
F	22	0	+	+	+	15			
G	42	22	3	+	32	18	45		
G	36	12	+	+	5	+	23	22	

‡ Adrenolytic effect of cyclopropane subsequently demonstrated in this dog.
+ Nodal rhythm or occasional extrasystole. 0 = No observed effect.
V.T. = Ventricular tachycardia.
V.F. = Ventricular fibrillation.

to produce ventricular tachycardia in three experiments (dogs A and E). In the remaining dogs there was reduction in the duration and severity of the epinephrine induced arrhythmias. In all dogs, 20 minutes after Syntocinon was administered, epinephrine still failed to produce arrhythmias as severe as the control. In two dogs (F and G), the Syntocinon appeared to mitigate the effects of epinephrine for 75 to 90 minutes. In one experiment (dog A) ventricular fibrillation and death occurred when the challenge dose of epinephrine was administered 30 minutes after Syntocinon. One animal (dog D) exhibited an adrenolytic action during cyclopropane anesthesia, this effect has been described by Stutzman and Allen (11). A return to the control level of ventricular tachycardia was eventually obtained in all the remaining dogs.

The experiment was repeated in three dogs under trichlorethylene anesthesia. In these animals Syntocinon appeared to protect the myocardium against the epinephrine induced arrhythmias for about 60 minutes, before the original sensitivity to epinephrine was regained.

The results are summarized in table 2.

Discussion

In the present study the dose of Syntocinon used was in excess of that recommended for clinical use (15, 16), but was chosen to compare with the doses of posterior pituitary extracts used by Parsloe, Morris and Orth (4). The fall in blood pressure seen in dogs, resembles that which these authors found to occur with Pituitrin, but was less pronounced and less persistent. They reported a rise in blood pressure with Pitocin. It is of interest to note that Francis and Francis (16) noted a slight increase in blood pressure with Syntocinon in unanesthetized patients. Unlike the effects seen with the posterior pituitary extracts under Cyclopropane anesthesia (4), none of the dogs in this study showed any abnormality of the electrocardiogram with Syntocinon.

In the second part of this study, it has been found that Syntocinon appears to mitigate the cardiac conduction effects of epinephrine in dogs anesthetized with cyclopropane and trichlorethylene. A similar observation has been made with Pituitrin (4), and has been observed with Pitocin during cyclopropane anesthesia (17).

From these results it would appear that Syntocinon administration is compatible with cyclopropane, trichlorethylene and barbiturate anesthesia. It appears to be free of pressor factor and to depress, to some extent, the myocardial irritability produced by cyclopropane and trichlorethylene.

Summary

The effects of Syntocinon administration during cyclopropane, trichlorethylene and barbiturate anesthesia have been investigated in

dogs. During cyclopropane anesthesia, Syntocinon caused a decrease in blood pressure in eight out of fifteen experiments, had no effect in five, and caused an increase in blood pressure twice. No electrocardiogram abnormalities were detected. During trichlorethylene anesthesia, Syntocinon caused a rise in blood pressure in the three experiments performed. Exaggerated sinus arrhythmia was observed once. During barbiturate anesthesia an increase in blood pressure occurred in two instances. No change was recorded in the third dog. Syntocinon appeared to afford some protection against epinephrine induced arrythmias under cyclopropane and trichlorethylene anesthesia.

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