Antiarrhythmic and Cardiovascular Effects of Synthetic Oxytocin

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Cardiac arrhythmias were produced in the cat by the inhalation of: (1) halopropene, (2) halopropene and 10 per cent carbon dioxide, (3) cyclopropane and 10 per cent carbon dioxide. The injection of 20 U/kg of Syntocinon temporarily restored a normal sinus rhythm. This dose of Syntocinon also prevented arrhythmias produced by the injection of norepinephrine during the inhalation of halopropene or cyclopropane. The antiarrhythmic dose of Syntocinon (10 or 20 U) was also demonstrated in 13 of 20 patients who developed cardiac arrhythmias during anesthesia and operation.

Syntocinon, in man, produced a transient (30–60 seconds) fall in blood pressure (20–40 mm. of mercury) and a secondary rise of 5–15 mm. of mercury which lasted 2–5 minutes. A 1–2 minute increase in heart rate of 10–20 beats/minute was frequently seen.

Although the effect of oxytocin on uterine smooth muscle is well established, its action on cardiac and vascular smooth muscle is less well understood. This study deals with (1) the effect of oxytocin on cardiac arrhythmias in the cat and dog; (2) a clinical trial of oxytocin in the treatment of cardiac arrhythmias occurring during anesthesia and operation; (3) the effect of oxytocin on the response of the cat to carotid occlusion and to some adrenergic and cholinergic agents.

Methods

Cat. Fifty-two cats weighing 2–4 kg. were studied. The antiarrhythmic action of oxytocin was determined in 22 of these cats. Each animal was placed in a clear plastic box with unidirectional valves to which a mixture of 10 per cent ether and 90 per cent oxygen was delivered from a Vernitrol anesthesia machine. When surgical anesthesia was established, the trachea, femoral artery and vein were cannulated. Needle electrodes were placed in the four limbs and lead 2 of the electrocardiogram recorded on a Grass polygraph. Femoral arterial pressure was measured with a Statham transducer and recorded on the polygraph. All injections were made into the femoral vein.

Once the surgical procedures were completed, and the blood pressure and electrocardiographic recordings began, the ether was discontinued and either halopropene or cyclopropane started. The anesthetic agent was delivered from a Vernitrol anesthesia machine by a nonrebreathing system (Frumin nonrebreathing valve). Succinylcholine 2 mg./kg. every 30 minutes or 0.1 mg./kg./minute or decamethonium 0.3 mg./kg. every 20 minutes was given intravenously and the animals artificially ventilated with a Harvard respirator. Control studies demonstrated that succinylcholine and decamethonium as given did not affect the results. To determine the adequacy of artificial ventilation and the effect of carbon dioxide inhalation, arterial blood samples were drawn for analysis of pH and Pco₂ (Astrup AME-1).

Cardiac arrhythmias were produced by the following procedures: (1) the inhalation of 1–2 per cent halopropene and 98–99 per cent oxygen; (2) the inhalation of 1 per cent halopropene, 10 per cent carbon dioxide and 89 per cent oxygen; (3) the injection of 1 μg./kg. of norepinephrine during the inhalation of 1 per cent halopropene and 99 per cent oxygen; (4) the inhalation of 20 per cent cyclopropane, 10 per cent carbon dioxide and 70 per cent oxygen; (5) the injection of 2–5 μg./kg. of norepinephrine during the inhalation of 20

Received from the Department of Anesthesiology and Department of Pharmacology, Columbia University, College of Physicians and Surgeons and the Anesthesiology Service, The Presbyterian Hospital, New York City. Accepted for publication April 8, 1964. This work was supported in part by Grant RG 9069 from the National Institute of General Medical Sciences of the National Institutes of Health.

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per cent cyclopropane and 80 per cent oxygen.

Thirty cats anesthetized with pentobarbital (36 mg./kg. intraperitoneally) were used to study the effects of oxytocin on the response to adrenergic and cholinergic agents and carotid occlusion. In these cats similar results were obtained with spontaneous or artificial ventilation. In 9 of these 30 cats the right chest was opened under artificial ventilation, and a Walton-Brodie strain gauge arch was sutured to the right ventricle for the measurement of myocardial contractile force.

**Dog.** Five dogs weighing 9–12 kg. were studied. Following the intravenous injection of 15 mg./kg. of thiamylal sodium the trachea, femoral artery and femoral vein were cannulated. A mixture of 1 per cent halopropane and 99 per cent oxygen was inhaled via the nonrebreathing system described above. Succinylcholine 0.01 mg./kg./minute was infused intravenously and the animals artificially ventilated with a Harvard respirator. Arterial pH, $P_{O_2}$, blood pressure and the electrocardiogram were recorded as described above. Arrhythmias were produced in the dog by the inhalation of 1 per cent halopropane, 10 per cent carbon dioxide and 89 per cent oxygen.

**Man.** Twenty patients who developed cardiac arrhythmias during anesthesia and operation and 10 patients with a normal sinus rhythm were studied. Prior to anesthesia the patients usually were given a barbiturate (50–100 mg. secobarbital or pentobarbital) and/or a narcotic (meperidine 50–100 mg.) and atropine 0.4–0.6 mg. or scopolamine 0.4–0.6 mg. Anesthesia was induced with 150–350 mg. thiopental sodium and maintained with halothane, methoxyflurane, trichlorethylene, cyclopropane or halopropane. The ECG was visually observed on an ORM-1 cardioscope and recorded on a Grass polygraph or Offner dynograph. Blood pressure was monitored by auscultation with the Riva-Rocci technique.

The following drugs were used: epinephrine hydrochloride, norepinephrine bitartrate, isoproterenol hydrochloride, ethyl-norepinephrine hydrochloride and acetylcysteine hydrochloride. The doses are expressed in terms of the salts except for norepinephrine bitartrate which is expressed in terms of the base. Syntocinon, available in a 1 ml. ampoule which contains 10 U of synthetic oxytocin, 2 mg. acetic acid, 1 mg. sodium acetate, 5 mg. ethanol and 5 mg. chlorobutanol was also used. Synthetic oxytocin as well as the vehicle (hereafter referred to as chlorobutanol) were studied separately.

**Results**

**Antiarrhythmic Action**

**Cats Given Halopropane.** In 13 of 17 cats arrhythmias were produced by the inhalation of 1–2 per cent halopropane and oxygen. The rhythm disturbance consisted predominately of frequent supraventricular and ventricular premature contractions. It was frequently difficult to distinguish supraventricular beats with aberrant conduction from those originating in a ventricular focus. The frequency of ectopic beats (number of ectopic beats per minute/total number of beats per minute) varied from 50–90 per cent (mean = 71 per cent). These arrhythmias persisted as long as the halopropane was inhaled (up to 8 hours). Discontinuing the halopropane restored a normal sinus rhythm in 5–30 minutes depending upon the prior duration of inhalation.

After the arrhythmia had persisted for at least 15 minutes and the frequency of ectopic
beats determined, Syntocinon 1–10 U/kg. was given intravenously. No significant reduction in the frequency of ectopic beats was observed with this dose of Syntocinon. However, 20 U/kg. restored a normal sinus rhythm in 10 of 13 cats (fig. 1). After 30 seconds to 4 minutes (mean = 110 seconds) of normal sinus rhythm a gradual return to the control frequency of ectopic beats occurred over the next 3–8 minutes (mean = 5 minutes). When the arrhythmia returned and persisted for at least 15 minutes, the injection of 20 U/kg. of Syntocinon was repeated and produced results similar to those seen with the first dose. In these 10 cats the arrhythmia was abolished at least three times by Syntocinon. In the remaining three cats Syntocinon decreased the frequency of ectopic activity but did not restore a normal sinus rhythm.

Four of the 17 cats maintained a normal sinus rhythm during halopropane anesthesia. Arrhythmias were induced in these animals by the inhalation of 10 per cent carbon dioxide or the intravenous administration of norepinephrine. The inhalation of 10 per cent carbon dioxide decreased the arterial pH from a control mean of 7.32 to 7.11 and raised \( P_{CO_2} \) from a control mean of 31 to 63 mm. of mercury. A constant level of acidosis was established by the inhalation of carbon dioxide for at least 10 minutes and the frequency of ectopic beats determined (65–90 per cent, mean = 80 per cent). Twenty U/kg. of Syntocinon restored a normal sinus rhythm in all 4 animals. After 30–120 seconds (mean = 65 seconds) a gradual return to the control frequency of ectopic beats occurred over the next 2–4 minutes. The carbon dioxide was then discontinued and a normal sinus rhythm observed for at least one hour before the cat was challenged with norepinephrine.

In these 4 cats who maintained a normal sinus rhythm during halopropane inhalation, the injection of 1 \( \mu g./kg. \) of norepinephrine produced ventricular arrhythmias of 1–4 minutes duration. The injection of 20 U/kg. of Syntocinon 5–10 seconds before norepinephrine prevented the increase in blood pressure after norepinephrine in 2 cats. Syntocinon did not modify the blood pressure response to norepinephrine in the other 2 cats. In all 4 however, Syntocinon prevented the norepinephrine-induced arrhythmias (fig. 2). When Syntocinon was given 15–60 seconds before the norepinephrine the onset of arrhythmia was delayed and the duration decreased. No consistent prevention of the arrhythmia was observed when the interval between Syntocinon and norepinephrine injections was greater than 60 seconds. In all 4 cats the antiarrhythmic effect of Syntocinon on halopropane-carbon dioxide and halopropane-norepinephrine arrhythmias was demonstrated at least twice.
Chlorobutanol (10 mg./kg.) was infused into 8 of the 17 cats described above. This agent had no effect on the halopropene, halopropene-carbon dioxide and halopropene-norepinephrine arrhythmias. Twenty U. kg. of synthetic oxytocin (without chlorobutanol) was tested against these three arrhythmias in 4 of these 17 cats. An antiarrhythmic effect similar to that of Syntocinon was seen.

Cats Given Cyclopropane. In 5 cats a normal sinus rhythm was maintained during the inhalation of 20 per cent cyclopropane and 80 per cent oxygen. However, the inhalation of 20 per cent cyclopropane, 10 per cent carbon dioxide and 70 per cent oxygen produced arrhythmias similar to those seen with halopropene. The frequency of ectopic activity was somewhat less (33–75 per cent, mean = 50 per cent). The injection of 20 U/kg. of Syntocinon restored a normal sinus rhythm for 60–180 seconds (mean = 120). A gradual return to the control frequency of ectopic beats occurred over 3–5 minutes. Carbon dioxide was then discontinued and a normal sinus rhythm observed for at least 1 hour before challenging the cat with norepinephrine.

The injection of 2–5 µg./kg. of norepinephrine produced ventricular arrhythmias of 1–2 minutes duration. The injection of 20 U/kg. of Syntocinon 5–10 seconds before the norepinephrine prevented the arrhythmias. When Syntocinon was given 1–3 minutes before the norepinephrine the onset of arrhythmia was delayed and the duration decreased. No consistent prevention of the arrhythmia was observed when the interval between Syntocinon and norepinephrine injections was greater than 3 minutes. The antiarrhythmic activity of Syntocinon on cyclopropane-carbon dioxide and cyclopropane-norepinephrine arrhythmias was demonstrated at least twice in each of the 5 cats studied. Chlorobutanol (10 mg./kg.) did not block the cyclopropane-carbon dioxide or cyclopropane-norepinephrine arrhythmias (3 cats). These arrhythmias were blocked in the 2 animals who received 20 U/kg. of synthetic oxytocin (without chlorobutanol).

Dog. Although arrhythmias were seen with halopropene and oxygen in the dog, they could not be produced consistently and frequently disappeared spontaneously. The addition of 10 per cent carbon dioxide to the inhaled mixture produced arrhythmias that persisted as long as the carbon dioxide was inhaled. Arrhythmias were produced in 5 dogs by the inhalation of 1 per cent halopropene, 10 per cent carbon dioxide and 89 per cent oxygen. The frequency of ectopic beats varied from 50–80 per cent (mean = 66 per cent). Injection of 3–5 U/kg. of Syntocinon restored a normal sinus rhythm for 2–11 minutes (mean = 5 minutes) (Fig. 3). A return to the control frequency of ectopic beats occurred over the next 5–8 minutes. In all 5 dogs the arrhythmia was abolished at least twice.

Man. Cardiac arrhythmias similar to those seen in the cat and the dog were observed during the course of anesthesia and operation in 20 patients ranging in age from 22 to 63. Arrhythmias occurred during inhalation of halothane (8 patients), halopropene (3), cyclopropane (5), methoxyflurane (2), trichloroethylene (2). The events associated with the arrhythmias were (a) adrenal manipulation (2 cases); (b) endotracheal intubation (2); (c) carbon dioxide retention (2); (d) reacting and straining on the endotracheal tube (2); (e) breath holding (1); (f) subcutaneous injection of 0.5 mg. epinephrine during cyclopro-
Fig. 4. Lead 2 of electrocardiogram during cyclopropane anesthesia in a 38 year old female patient. (A) Control record after 10 minutes of anesthesia. (B) Arrhythmia following subcutaneous infiltration of 0.5 mg. epinephrine. (C) Note increase in number of ectopic foci after injection of Syntocinon. (D) Normal sinus rhythm restored one minute remainder of operation. (E), (F), (G) Persistence of normal sinus rhythm for 30–120 seconds. Subsequent doses of Syntocinon regardless of the amount produced smaller increases in pressure (5–40 mm. of mercury). The rise in diastolic pressure was usually 5–15 mm. of mercury greater than the rise in systolic pressure. The heart rate was unchanged. The myocardial contractile force was either unchanged by oxytocin or increased slightly secondary to a marked increase in blood pressure.

Chlorobutanol (10 mg./kg.) given intravenously decreased the systolic and diastolic pressure in the cat by 25–50 mm. of mercury for 30–150 seconds. Smaller doses of chlorobutanol also decreased the blood pressure. The smallest dose of chlorobutanol producing a fall in blood pressure of 15 mm. of mercury was 0.5 mg./kg. The heart rate decreased 20–30 beats/minute. The myocardial contractile force was unchanged or decreased slightly after a marked fall in blood pressure.

Syntocinon produced variable changes in blood pressure; 20 U/kg. produced an increase, decrease or no change in systolic and diastolic pressure. The blood pressure response in a given animal appeared to depend upon the magnitude of increase produced by synthetic oxytocin (without chlorobutanol) and the magnitude of fall produced by chlorobutanol. The heart rate usually decreased 15–30 beats/minute without regard to the blood pressure response. Myocardial contractile force was unchanged or varied in the same direction as a major change in blood pressure.

Blood Pressure and Heart Rate Effects

Cat. Synthetic oxytocin (without chlorobutanol also decreased the blood pressure in the cat. The first dose whether 1, 2, 5, 10 or 20 U/kg. produced a rise in systolic and a fall in blood pressure of 15 mm. of mercury for 30–120 seconds. Subsequent doses regardless of the amount produced smaller increases in pressure (5–40 mm. of mercury). The rise in diastolic pressure was usually 5–15 mm. of mercury greater than the rise in systolic pressure. The heart rate was unchanged. The myocardial contractile force was either unchanged by oxytocin or increased slightly secondary to a marked increase in blood pressure.

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Fig. 5. Effect of oxytocin (Syntocinon 20 U/kg.) on the blood pressure response to 50 μg./kg. ethylnorepinephrine (ENE), 1 μg./kg. isoproterenol (ISOP) and 1 μg./kg. epinephrine (EPI). (A) Cat 11/63, 2.5 kg. Left panel: Fall in blood pressure produced by ENE. Right panel: One minute after 20 U/kg. Syntocinon. Note ENE reversal. (B) Cat 12/63, 2 kg. Left panel: Fall in blood pressure produced by ISOP. Right panel: 2 minutes after 20 U/kg. Syntocinon. Note diminution of depressor response to ISOP. (C) Cat 13/63, 3.2 kg. Left panel: Biphasic blood pressure response after EPI. Right panel: 2 minutes after 20 U/kg. Syntocinon. Note greater pressure response and absence of depressor response.

Man. The effects of Syntocinon and synthetic oxytocin (without chlorobutanol) on blood pressure and heart rate were studied in 10 patients (5 in each group) with normal sinus rhythm. Each patient received 3 injections of 10 U of the agent at 10-minute intervals. The blood pressure and heart rate changes in these 10 patients were not significantly different and were similar to those seen in the 20 patients with arrhythmias described above. In 26 of the 30 patients the first dose of the agent produced a transient (30–60 seconds) fall in blood pressure (20–40 mm. of mercury). A secondary rise of 5–15 mm. of mercury lasting 2–5 minutes was observed in 18 of the 30 patients. An increase in heart rate of 10–20 beats, minute lasting 1–2 minutes was noted in 27 of 30 patients. In those patients receiving more than one injection of Syntocinon or synthetic oxytocin (without chlorobutanol) subsequent doses produced lesser falls in blood pressure. In 4 patients although no change in blood pressure was noted on the third dose an increase in heart rate was observed.

Syntocinon and synthetic oxytocin (without chlorobutanol) produced no significant electrocardiographic changes other than the antiarrhythmic action and occasional flattening of the T wave (6 of 30 patients).
EFFECTS OF SYNTHETIC OXYTOCIN

The carotid occlusion response of the cat was either abolished or markedly diminished for 1–3 minutes after Syntocinon (20 U/kg.) or chlorobutanol (10 mg./kg.). A return toward the control response occurred within ten minutes. The carotid occlusion response was not affected by 20 U/kg. of synthetic oxytocin (without chlorobutanol).

Discussion

An antiarrhythmic action of oxytocin has been previously demonstrated in laboratory animals. The types of cardiac arrhythmias produced and the doses of oxytocin required to block the arrhythmias have varied. Feldman et al.\(^1\) used 1 U/kg. to block cyclopropane-epinephrine and trichlorethylene-epinephrine arrhythmias in the dog. Panisset and Beaulnes\(^2\) blocked chloroform-epinephrine arrhythmias in the dog with 1 U/kg. of oxytocin. They also demonstrated an antiarrhythmic action on: (1) atrial arrhythmias induced in isolated rabbit atria by electrical stimulation, administration of acetylcholine and lowering of potassium concentration; (2) ventricular arrhythmias produced by electrical stimulation of the isolated perfused rabbit heart. Covino\(^3\) found that 2 U/kg. of oxytocin did not prevent ventricular fibrillation in hypothermic dogs, but a continuous infusion of 1 U/kg./minute was effective.

Oxytocin is also capable of blocking centrally induced cardiac arrhythmias. Melville and Varma\(^4\) found in the rabbit that 2 U/kg. of oxytocin reversed ventricular fibrillation produced by injecting 0.1 mg. of picrotoxin into a lateral cerebral ventricle. Bircher et al.\(^5\) used 0.1–1.2 U/kg. of oxytocin intravenously to block arrhythmias induced by injecting pentylentetrazol, picrotoxin and deslanoside into the cerebral ventricle of the dog.

The dose of oxytocin required to block the halopropane-carbon dioxide arrhythmias in our dog studies (3–5 U/kg.) is less than that required by Covino\(^3\) but greater than that required by others.\(^1,2,5\) Since the same experimental animal (dog) was used in the different studies, the type of arrhythmia studied may account for the variation in effective dose.

In our studies on the cat, oxytocin (20 U/kg.) demonstrated an antiarrhythmic action...
when tested against halopropane, halopropane-carbon dioxide, halopropane-norepinephrine, cyclopropane-carbon dioxide, and cyclopropane-norepinephrine induced arrhythmias. Oxytocin was tested against these five arrhythmias because they are similar to those seen in man. These arrhythmias differ quantitatively and qualitatively. These differences can be seen in terms of ease of production, frequency of ectopic beats and variation in response to surgical and drug treatment of the arrhythmias. 6

Although an antiarrhythmic action of oxytocin could be demonstrated in anesthetized patients, its ultimate general usefulness in man would seem limited because of the brief duration of action and the development of tachyphylaxis. Analogues of oxytocin are under investigation in an attempt to find a compound of possible wider therapeutic value.

Neither the site nor mechanism of antiarrhythmic action of oxytocin is known. Melville and Varma1 demonstrated in the rabbit that oxytocin (1-2 U/kg.) reversed the ECG observed ST-T depression induced by hypoxia and suggested a metabolic action of oxytocin enabling the heart to utilize oxygen more effectively. This hypothesis has not to our knowledge been tested. Panisset and Beauches2 suggested a quinidine-like action of oxytocin. Unlike quinidine which raises the threshold, prolongs the refractory period, and decreases the conduction velocity of the ventricle, oxytocin, according to Covino3 has no effect on the threshold or conduction velocity of papillary muscle, but does prolong the refractory period. He believed that this effect was probably responsible for the antiarrhythmic effect in hypothermia, but was not certain as to whether the prolongation of the refractory period could account for its action against other experimental arrhythmias.

The arrhythmias produced in the cat are blocked by the alpha and beta adrenergic blocking agents. 6 Therefore oxytocin was investigated for possible adrenergic or cholinergic blocking action. Oxytocin did not modify the blood pressure response to norepinephrine or acetylcholine, but ENE reversal and a diminution of the depressor response to ISOP was observed. Modification of the blood pressure response to ENE and ISOP is evidence for beta adrenergic receptor blockade if the agent producing these effects is not a vasoconstrictor. 7-8 If the agent in question is a vasoconstrictor these effects are believed to be manifestations of the cardiac stimulating effects of ENE and ISOP in the presence of a constricted vascular bed which is incapable of being dilated by ENE or ISOP. 7-8 Since 20 U/kg. synthetic oxytocin (without chlorobutanol) consistently raises the blood pressure in the cat, it seems likely that in this species oxytocin is a vasoconstrictor and modifies the response to ENE and ISOP by this action rather than by beta adrenergic blockade. The absence of a chronotropic and inotropic blocking action of oxytocin supports this concept.

In man the blood pressure and heart rate changes with Syntocinon and synthetic oxytocin (without chlorobutanol) were similar, presumably because of the small amount of chlorobutanol involved. The blood pressure fell transiently and then returned to normal or slightly above normal. Associated with the fall was an increase in heart rate which was also brief in duration. The increase in heart rate is probably not reflex in nature since it was seen whether or not the blood pressure fell. Although a transient fall in blood pressure has been reported by many observers,9-11 its mechanism has been disputed. Woodbury et al.,9 who used Pitocin, believed that the fall in blood pressure was not due to peripheral vasodilation and attributed the hypotension to a weakness of cardiac contraction and a fall in cardiac output. More recent studies in which cardiac output, and blood flow in the hand and forearm were measured, demonstrated that Syntocinon in man had a vasodilator action which was associated with a fall in blood pressure and a rise in cardiac output.10 Similar findings were also reported by Bieniarz.11

Chlorobutanol, the preservative in Syntocinon and Pitocin is pharmacologically quite active. It has been used as an oral hypnotic agent in man (300-1,200 mg.).14 In the dog 200 mg./kg. intraperitoneally or by stomach tube produces anesthesia of several hours duration.15 Chlorobutanol also produces local anesthesia, hypotension and a decrease in the
respiratory center response to carbon dioxide. The variable blood pressure effects of Syntocin on in the cat were difficult to interpret until synthetic oxytocin (without chlorobutanol) was obtained and compared with Syntocin on and with chlorobutanol. Chlorobutanol lowered the blood pressure while oxytocin raised it. The response to Syntocin therefore depended upon the relative change produced by each agent. Abolition of the carotid occlusion response proved to be due to chlorobutanol and not oxytocin. Since in the cat as little as 0.5 mg./kg. of chlorobutanol could produce a fall in blood pressure, one wonders about the possible pharmacological effects of chlorobutanol in previous studies of the physiological and pharmacological actions of Syntocinon and Pitocin.

Summary

Cardiac arrhythmias were produced in the cat by the inhalation of: (1) halopropane, (2) halopropane and 10 per cent carbon dioxide, and (3) cyclopropane and 10 per cent carbon dioxide. The injection of 20 U/kg. of Syntocinon temporarily restored a normal sinus rhythm. This dose of Syntocinon also prevented arrhythmias produced by the injection of norepinephrine during the inhalation of halopropane or cyclopropane.

The antiarrhythmic action of Syntocinon (10 or 20 U) was also demonstrated in 13 of 20 patients who developed cardiac arrhythmias during anesthesia and operation.

Syntocinon had a variable effect on blood pressure in the cat. The blood pressure response in a given animal appeared to depend upon the magnitude of fall in pressure produced by chlorobutanol (the preservative in Syntocinon) and the magnitude of rise produced by synthetic oxytocin (without chlorobutanol). In man Syntocinon produced a transient (30–60 seconds) initial fall in pressure (20–40 mm. of mercury) and a secondary rise of 5–15 mm. of mercury lasting 2–5 minutes. A 1–2 minute increase in heart rate of 10–20 beats/minute was frequently seen.

Syntocinon produced ethylnorepinephrine reversal and diminished the depressor response to isoproterenol in the cat. These effects appeared to be due to a vasoconstrictor action rather than a true beta adrenergic blockade. Abolition of the carotid occlusion response of the cat by Syntocinon proved to be due to chlorobutanol and not to synthetic oxytocin (without chlorobutanol).

Syntocinon, chlorobutanol and synthetic oxytocin (without chlorobutanol) were provided by Sandoz Pharmaceuticals, and Butanephrine (ethylnorepinephrine), by Sterling-Winthrop Research Institute.

References