EFFECT OF CYCLOPROPANE AND VARIOUS OXYTOCICS ON CARDIAC RHYTHM IN THE PARTURIENT WOMAN

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POSTERIOR pituitary preparations used as oxytocics at parturition have been reported to cause deleterious cardiovascular effects,[1-7] some of which have resulted in death.[4] Since many of these accidents have occurred when anesthetics were being used, it was hypothesized that the adverse effects might be due to an incompatibility between the oxytocic and the anesthetic drug.[4, 6, 7] Cyclopropane has been especially suspect.[4, 8, 9] In an effort to determine whether such incompatibility exists Parsloe, Morris and Orth [10] studied the effects of various pituitary fractions combined with several anesthetic agents in laboratory animals. They observed that general anesthesia decreased the incidence of deleterious cardiac effects caused by pituitrin in dogs. They postulated that since cardiac dysfunction from pituitrin was more marked in unanesthetized or lightly anesthetized animals, especially in the presence of myocardial hypoxia, that changes in cardiovascular status would be most likely seen "during recovery from an anesthetic, when (a) pituitrin has been administered just shortly before; (b) obstruction (retching) is most likely, and (c) some toxic agent (anesthetic) is still present in the myocardium." Their study showed the absence of potentiation or incompatibility between pituitrin and cyclopropane, and emphasized the advantages of pitocin since no serious deleterious effects on blood pressure and cardiac rhythm were observed following its use.

In order to test the clinical applicability of these observations and conclusions, Morris, Thornton and Harris [11] studied the electrocardiographic changes following use of pituitrin, pitocin and ergonovine during cyclopropane anesthesia in pregnant women at parturition. Fewer ventricular arrhythmias were seen following pitocin or ergonovine than after pituitrin. On the basis of these findings plus the preceding laboratory study it was suggested that pituitrin be avoided in clinical practice in favor of the less toxic pitocin.

Two case reports have appeared in which death occurred subsequent to the administration of "pitocin" for induction of labor.[12, 13] One of these followed an examination of a patient with placenta previa who had not fully recovered from cyclopropane anesthesia.[13] Since deaths have occurred under similar circumstances during recovery from anesthesia and without the concomitant use of pitocin, it may be questioned whether a cause and effect relationship existed. However, the authors who reported the case [13] believed that death was most likely due to a coronary constrictor effect of vasopressin contaminating the pitocin in a patient whose coronary arteries were found at autopsy to have excessive atheromata.

A new chemically pure oxytocic, Syntocinon, has been synthesized and introduced into obstetric practice.[14, 15] Syntocinon possesses similar pharmacological effects to those of pitocin.[16-21] In order to investigate the safety of Syntocinon with anesthetics, Feldman, Forgaard and Morris [22] conducted a study in dogs anesthetized with cyclopropane, trichlorethylene, or barbiturates. They concluded that cyclopropane could be safely used with Syntocinon, since in their study only slight changes in blood pressure and occasional sinus bradycardia were found.

In order to further investigate and compare the effects of Syntocinon and pitocin on cardiac rhythm during cyclopropane anesthesia, this clinical study was undertaken.

METHOD

The study was conducted in a manner similar to that used by Morris, Thornton and Harris [11] except in the mode of administration of drugs. Their patients received drugs intra-

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muscularly, where as in this study drugs were given intravenously.

Observations were made during anesthesia and delivery of 72 obstetrical patients. Fifty-seven of these received either 10 units of Syntocinon alone or 10 units of Syntocinon followed at a later time by 0.2 mg. of Ergotrate (ergonovine maleate); 15 patients received either 10 units of pitocin alone or 10 units of pitocin followed later by 0.2 mg. of Ergotrate. Syntocinon or pitocin was given immediately after delivery of the placenta allowing approximately 30 seconds for injection. In about one-half of all cases Ergotrate was administered 15 to 30 minutes subsequently because of the obstetrician's preference.

In every instance electrocardiograms were taken before and during the administration of oxytocics and for at least 10 minutes afterwards. In the majority of patients standard leads were obtained before anesthesia and single lead at one minute intervals throughout the procedure and recovery period until the patient responded to questioning. The direct writing stylus of the Sanborn Visocardiette was continuously observed and, besides recording at one-minute intervals as mentioned, tracings were taken continuously for the first two minutes following the administration of oxytocics as well as whenever there was suspicion an abnormality was present.

Cyclopropane was given by members of the Anesthesia Department. Patients were unselected and represented about 25 per cent of the deliveries during the period of study. The obstetrical routine was not altered. For the purpose of the study more patients than usual received cyclopropane.

Because the incidence of arrhythmias is believed to increase during deep cyclopropane anesthesia,[23] anesthesia was maintained in the first plane of the third stage as judged by clinical signs. Efforts were made to avoid hypoventilation or respiratory obstruction since an increased incidence of arrhythmias during cyclopropane anesthesia in the presence of hypercarbia and/or hypoxia has been repeatedly reported.[23–26]

Four of the patients studied were delivered by Cesarean section. Forceps were used in 23 instances. There were two sets of twins. In two patients pre-eclampsia was suspected. In

TABLE 1

ELECTROCARDIOGRAPHIC IRREGULARITIES OBSERVED AFTER ADMINISTRATION OF SYNTOCINON OR PITOCIN DURING CYCLOPROPANE ANESTHESIA FOR PARTURITION

	Total Number of Patients in Each Group	Absence of Irregularities	SAT	SAB	SABl	SAExS	Wandering Pacemaker	AVR	AVExS	AVBl	PVC	VT	Others
Before drugs	57	15	23	9	2	6	12	2	1	4	4		
Syntocinon	24	8	5	5		2	5		1	3	4		
Syntocinon and Ergotrate	33	6	15	10		1	7			2	1	1	
Before drugs	15	9	4	1		1				1			
Pitocin	11	3	5	3		1	1			2	1		1*
Pitocin and Ergotrate	4		2	1		1	1				1		

SAT—Sinoatrial tachycardia, defined as a rate of 100 or more per minute.
SAB—Sinoatrial bradycardia, defined as a rate of 60 or less per minute.
SABl—Sinoatrial block.
SAExS—Sinoatrial extrasystole.
AVR—Atrioventricular nodal rhythm.
AVExS—Atrioventricular extrasystole.
AVBl—Atrioventricular block.
PVC—Premature ventricular contraction.
VT—Ventricular tachycardia.

* Marked alternation of the amplitude of the QRS complexes and T waves.

TABLE 2

ELECTROCARDIOGRAPHIC IRREGULARITIES TABULATED AFTER EXCLUDING ALL CASES IN WHICH RESPIRATORY OBSTRUCTION WAS NOTED

	Total Number of Patients in Each Group	Absence of Irregularities	SAT	SAB	SABl	SAExS	Wandering Pacemaker	AVR	AVExS	AVBl	PVC	VT	Others
Before drugs	47	13	20	9	1	6	8	1	1	4	1		
Syntocinon	19	8	4	2		2	4			2	1		
Synotcinon and Ergotrate	28	6	13	9		1	5			2			
Before drugs	14	8	4	1		1				1			
Pitocin	10	3	4	3		1	1			2	1		
Pitocin and Ergotrate	4		2	1		1	1				1		

SAT—Sinoatrial tachycardia, defined as a rate of 100 or more per minute.
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no patients was there evidence of pre-existing heart disease. In two patients labor had been induced with Syntocinon drip of one unit per 100 ml. concentration.

RESULTS

The frequency with which each of the observed cardiac irregularities occurred is presented in table 1. These data were submitted to statistical analysis by the Chi square method. No significant difference was observed in the incidence of ventricular irregularities after intravenous Syntocinon compared with pitocin, nor was there any difference in the incidence of irregularities after oxytocics compared with the period preceding their administration. Neither was there a significant increase in irregularities observed as compared with previous studies during cyclopropane anesthesia in which no oxytocics were administered.[27, 28]

In order to exclude as nearly as possible the effect of hypercarbia and hypoxia all cases exhibiting respiratory obstruction or hypoventilation were excluded from consideration. The irregularities noted in the remaining cases are presented in table II. In these latter cases there was no significant difference in the occurrence of either supraventricular or ventricular irregularities between Syntocinon and pitocin groups.

DISCUSSION

While evidence of respiratory obstruction or hypoventilation is frequently accompanied by cardiac irregularities, it seems of interest to comment that in four of seven cases in this study in which arrhythmias of ventricular origin occurred obvious obstruction was present. Of the three other cases one exhibited ventricular premature contraction prior to anesthesia. Unrecognized hypercarbia and hypoxia may have existed in the other two cases.

Pituitrin and pitressin have been condemned [11] because of the possibility of hypercarbia and hypoxia due to frequent episodes of retching and vomiting after its administration [29, 30] with consequent disturbance of respiration, whereas pitocin does not produce similar respiratory obstruction or deleterious cardiovascular effects.[10, 31] No patient in either the Syntocinon or pitocin group in this study retched or vomited in the 10 minute period after the administration of the drugs.

The main advantage of Syntocinon as com-

pared with pituitrin appears to be its lack of vasopressor principle,[32, 33] and thus the absence of the coronary constrictor effect reported with pituitrin[34] and pitressin.[35–37] Little has been reported of the cardiovascular effects of Syntocinon in the human being. Mayes and Shearman[18] noted, in three of four cases studied following intravenous injection of 2–5 units of Syntocinon, a transient flattening of the T waves in the electrocardiogram returning to normal within three minutes. Woodbury *et al.*[31] observed in three of four subjects that the injection of 3 units of pitocin caused a transient flattening of the T waves returning to normal within two or three minutes.

In the present study 47 per cent of the Syntocinon group and 33 per cent of the pitocin group showed a transient flattening of the T waves lasting an average of less than one minute. All patients in this series, however, received 10 units of Syntocinon or pitocin which was greater than the doses used by Mayes and Shearman or by Woodbury *et al.*

It appears from previous studies that pituitary extracts containing a vasopressor fraction in addition to the oxytocic fraction should be scrupulously avoided in clinical obstetric practice. Since pitocin is a biologic preparation separated from pituitary extract it is recognized that it may also contain some vasopressin.[39] This may explain the few reports of untoward results associated with the use of pitocin. However, in the electrocardiographic studies reported here no significant deleterious effects were observed that could be attributed to either pitocin or Syntocinon.

Summary

The effects of the intravenous administration of the oxytocics, Syntocinon and pitocin, on cardiac rhythm during cyclopropane anesthesia have been investigated electrocardiographically in 72 obstetrical patients at delivery. Under the conditions of the investigation there was no difference in the incidence of cardiac irregularities between the Syntocinon and pitocin groups. Both drugs were used safely with cyclopropane without the sequela of serious cardiac irregularities.

Syntocinon used in this study was supplied by Sandoz Pharmaceuticals.

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