THE CARDIAC EFFECT OF EPINEPHRINE DURING ANAESTHESIA IN HYPERTHYROID DOGS*

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PATIENTS WITH HYPERTHYROIDISM may develop symptoms and signs of severe toxicity during, or in association with, anaesthesia and surgery. These symptoms may vary from mild tremors and severe tachycardia to full-blown thyroid storm.[1] Most frequently, the disease causes an abnormal cardiac rate or rhythm.[2,3,4] Murray and his associates demonstrated that an epinephrine challenge is well tolerated by a euthyroid patient, but it causes marked discomfort to the hyperthyroid individual.[5] High spinal anaesthesia has been used by some to deafferent the adrenals, while others have used hypothermia and neuroplegics in preparing their patients for thyroidectomy, in order to reduce the amount of catecholamines in the circulation.[6,7,8] This study was undertaken to determine whether or not the hyperthyroid state alters the response to a standard epinephrine challenge during anaesthesia in dogs.

METHOD

Thirty mongrel dogs were studied. They were divided into three groups of ten dogs each. Group I dogs, weighing from 14 to 28 kg. (mean 22 kg.), were fed ground dog meal containing Protamone® (iodinated casein with 1 per cent free iodide and 7 per cent protein-bound iodine). Protamone 0.1 per cent by weight was mixed with the dog meal for the first period of nine days, 0.3 per cent Protamone for the next six days, and 0.6 per cent Protamone for the next seven to ten days. Protein-bound iodine determinations were done by Hycel technique before the dogs were placed on the Protamone-enriched diet, once during the feeding interval, and again on the day of the test.[9]

Anaesthesia was induced with a sleep dose of thiopental and 20 mg. of succinylcholine chloride to facilitate endotracheal intubation. An infusion of isotonic saline was started at this time to maintain hydration and provide a route for the injection of the epinephrine challenge.

Breathing was augmented with a Takaoka respirator for the maintenance of adequate pulmonary ventilation.[10] The volume of ventilation was set so that the animal would receive a minute volume of 400 ml./kg. body weight. Immediately following endotracheal intubation, an electrocardiogram (lead 2) was recorded on each dog while the animal was being ventilated with 100 per cent oxygen. Following the control tracing, 1 per cent methoxyflurane with oxygen was delivered to the dog from a temperature-compensated vaporizer (Pentec®). At five-minute intervals, an electrocardiogram tracing was taken until twenty-five minutes of methoxyflurane anaesthesia had elapsed. Then, an intravenous

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challenge with 0.02 mg. of epinephrine/kg. body weight was administered in a solution containing 0.02 mg./ml., injected at the rate of 1 ml./sec. The electrocardiogram tracing was recorded until it returned to the pre-injection configuration or the dog died of ventricular fibrillation.

The second group, weighing from 11 to 19 kg. (mean 16 kg.), was anaesthetized with thiopental 25 mg./kg. body weight and 20 mg. of succinylcholine chloride. After endotracheal intubation, the dogs were ventilated with 100 per cent oxygen until a base-line EKG had been recorded. Then, the volume of ventilation was set at 400 ml./kg. body weight/minute with nitrous oxide – oxygen in a ratio of 2:1. At the end of twenty-five minutes of anaesthesia, they were challenged as was the first group.

Survivors of this experiment were then fed a diet including Protamone, as described in Group I. Those dogs that died during the feeding period were replaced. After three weeks on the diet, they were again anaesthetized by the same technique with thiopental – nitrous oxide and challenged with epinephrine.

The third group (7 fresh dogs and 3 survivors of Group II) were fed as in Group I. Survivors of Group II were given a week of rest before repeat of anaesthesia. The dogs were anaesthetized and challenged with epinephrine as described for Group I except that 4.8 per cent trifluoroethylvinyl ether was used instead of methoxyflurane.

After a one-week rest, two survivors of Group III were anaesthetized with 2 per cent halothane in oxygen, after the previously described anaesthetic preparation. One dog was given the standard epinephrine challenge as above and one was given one-half the dose.

Results

The type, incidence, and duration of cardiac arrhythmias that occurred after epinephrine challenge are summarized in Tables I and II.

When the experiments were performed, there was a 10 per cent, 13 per cent, and 2 per cent mean reduction in body weight of the dogs in Groups I, II, and III respectively, in the hyperthyroid state. At this time, the weights for Group I were between 13.5 and 25 kg. (mean 20.1 kg.); for Group II, between 11 and 25 kg. (mean 16.9 kg.); and for Group III, between 9.5 and 20 kg. (mean 12.6 kg.).

The mean basal P. B. I. was 2.7 ± 0.4 $\mu g.\%$. On the day of the acute experiment, the P. B. I. was in excess of 11.3 $\mu g.\%$ in all the dogs that were fed with Protamone.

The mean heart rate after endotracheal intubation, for Group I, was 174 ± 42 beats/minute; for Group II euthyroid dogs, it was 192 ± 33 beats/minute, and for the hyperthyroid dogs 208 ± 33 beats/minute; for Group III, it was 196 ± 37 beats/minute. After twenty-five minutes of anaesthesia with methoxyflurane, the average heart rates decreased to 155 ± 63 beats/minute for Group I. The average heart rate for Group II dogs anaesthetized with thiopental – nitrous oxide decreased to 131 ± 39 beats/minute for the euthyroid dogs and to 161 ± 38 beats/minute for the hyperthyroid dogs. The heart rate of the hyperthyroid dogs in Group III anaesthetized with trifluoroethylvinyl ether slowed to 164 ± 53 beats/minute.

TABLE I

Group No.	No. of dogs	Anaesthetic agent	Ventricular fibrillation	Ventricular premature contractions	Ventricular tachycardia	Bigeminy	Ventricular rhythm	Multifocal ventricular extrasystoles
I. Hyperthyroid	10*	Methoxyflurane	4	6	5	6	6	5
II. Euthyroid	10*	Thiopental – nitrous oxide	1	9	7	7	7	7
Hyperthyroid	10*	Thiopental – nitrous oxide	5	5	5	3	5	5
III. Hyperthyroid	10*	Trifluoroethylvinyl ether	4	6	5	4	6	5
Hyperthyroid	2†	Halothane	1	1	1	0	1	1

*If dogs sustained ventricular fibrillation, no other arrhythmias were included
†The dog that survived received one-half the epinephrine challenge.

TABLE II

MEAN DURATION OF ARRHYTHMIAS DUE TO EPINEPHRINE CHALLENGE IN BOTH EUTHYROID AND HYPERTHYROID DOGS

Group No.	No of dogs	Anaesthetic agent	Onset of arrhythmias (seconds after epinephrine)	Duration of ventricular tachycardia (seconds)	Total duration of arrhythmias (seconds)
I. Hyperthyroid	10*	Methoxyflurane	12 7	51	128
II. Euthyroid	10*	Thiopental – nitrous oxide	13 2	116	186
Hyperthyroid	10*	Thiopental – nitrous oxide	11 4	48	99
III. Hyperthyroid	10*	Trifluoroethylvinyl ether	9 4	55	108
Hyperthyroid	2†	Halothane	15 8	6	147

*Only dogs who did not have ventricular fibrillation are included in the calculation of duration of arrhythmias.
†One dog received 0 01 mg /kg. body weight/second of epinephrine as a test (other dog, ventricular fibrillation)

All of the dogs studied developed severe ventricular arrhythmias after the epinephrine challenge, except two euthyroid dogs. Five hyperthyroid dogs anaesthetized with thiopental – nitrous oxide sustained ventricular fibrillation whereas previously in the euthyroid state only one of this group of animals developed ventricular fibrillation. Four hyperthyroid dogs anaesthetized with methoxyflurane, and four with trifluoroethylvinyl ether, developed ventricular fibrillation.

Five hyperthyroid dogs anaesthetized with methoxyflurane, and five with trifluoroethylvinyl ether, developed ventricular tachycardia with an average duration of 51 and 55 seconds respectively. One dog anaesthetized with each drug had a severe tachycardia before epinephrine challenge; the heart rates did not increase appreciably after the epinephrine although there was ECG evidence of ventricular rhythm and premature ventricular contractions. During thiopental – nitrous oxide anaesthesia, seven euthyroid dogs developed ventricular tachycardia of 117 seconds average duration, and five of the hyperthyroid dogs developed ventricular tachycardia of 48 seconds average duration.

The mean duration of the arrhythmias seen in the surviving animals was 128 seconds for Group I; 186 seconds and 99 seconds respectively for the euthyroid and hyperthyroid dogs of Group II; and 108 seconds for Group III.

Discussion

In hyperthyroid dogs, there is no demonstrable increase in epinephrine entering the blood stream from the adrenal glands,[11] although the heart appears to become more sensitive to epinephrine.[5]

In dogs with total chemical sympathetectomy, the heart rate during "hyperthyroidism" falls to the same level as in euthyroid dogs similarly treated.[12] Therefore it appears certain that there is no increase in epinephrine production, but rather an increased duration of action of circulating epinephrine, possibly because its oxidation is reduced, on account of a decrease in circulating amine oxidase.[13, 14]

The arrhythmias seen in "hyperthyroid" dogs during anaesthesia with 1 per cent methoxyflurane, 4.8 per cent trifluoroethylvinyl ether, and given a standard dose of epinephrine, are much more severe than previously reported in euthyroid dogs, or in this series with euthyroid dogs during thiopental – nitrous oxide anaesthesia.[15–18] There were no spontaneous arrhythmias seen in any of the "hyperthyroid" animals prior to the epinephrine challenge.

With a smooth induction and well-conducted anaesthesia, a hyperthyroid individual might have no difficulty. On the other hand, if there is inadequate premedication, or if respiratory obstruction or carbon dioxide retention is allowed to develop, and the endogenous catecholamine level in the blood rises, the hyperthyroid patient is more likely to develop serious cardiac arrhythmias.

The dogs anaesthetized with thiopental – nitrous oxide had the same incidence of arrhythmias in the euthyroid state as has been seen previously with methoxyflurane and trifluoroethylvinyl ether.[15, 17, 18] In the hyperthyroid state, the dogs anaesthetized with methoxyflurane and trifluoroethylvinyl ether had a similar

incidence of severe arrhythmias to those anaesthetized with thiopental – nitrous oxide.

Summary and Conclusions

In this study, it was assumed that a true hyperthyroid state could be produced in dogs by the oral administration of Protamone until the protein-bound iodine level in the blood was markedly elevated. Dogs made "hyperthyroid" in this way were given a standard epinephrine challenge during methoxyflurane, trifluoroethylvinyl ether, and thiopental – nitrous oxide anaesthesia. Ventricular fibrillation occurred more frequently and the quality and severity of arrhythmias were greater than was seen in euthyroid dogs after a similar challenge with epinephrine. Euthyroid dogs during thiopental – nitrous oxide anaesthesia were subjected to the standard epinephrine challenge. The qualitative and quantitative arrhythmias resulting were the same as previously reported with methoxyflurane and trifluoroethylvinyl ether.

These experiments suggest that the risk of cardiac arrhythmias during clinical anaesthesia in the hyperthyroid patient is probably the same with methoxyflurane, trifluoroethylvinyl ether or thiopental – nitrous oxide, and that the use of epinephrine during such anaesthesias may be as dangerous as with halothane.

Résumé

Au cours de cette étude, nous avons présumé pouvoir produire un état d'hyperthyroïdie vraie chez des chiens en leur administrant par la bouche de la Protamone jusqu'à ce que le taux d'iode lié aux protéines du sang soit élevé de façon marquée. Les chiens ainsi rendus hyperthyroïdiens ont été soumis à un test standard à l'épinéphrine au cours d'une anesthésie soit au méthoxyflurane, soit à l'éther trifluoroéthylvinyl, soit au protoxyde et pentothal. Nous avons observé des fibrillations ventriculaires plus fréquentes et des arythmies plus graves que chez les chiens euthyroïdiens témoins soumis au même test. Au cours de l'anesthésie au protoxyde d'azote et pentothal chez les témoins euthyroïdiens, nous avons pratiqué le même test standard à l'épinéphrine. Les arythmies observées étaient les mêmes en qualité et en quantité que celles notées au préalable au cours de l'anesthésie au méthoxyflurane et au trifluoroéthylvinyl éther.

Ces expériences nous font croire que le risque des arythmies cardiaques durant l'anesthésie clinique chez l'hyperthyroïdien est probablement le même avec le méthoxyflurane, le trifluoroéthylvinyl éther ou le protoxyde d'azote et le pentothal, et que l'emploi de l'épinéphrine au cours de semblables anesthésies peut être aussi dangereux qu'avec le fluothane.

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