Date:

Title : ARRHYTHMOGENICITY OF TERBUTALINE IN ANESTHETIZED DOGS

Authors : R.R. Little, M.D., C.C. Hug, Jr., M.D., Ph.D. and E.L. Frederickson, M.D.

Affiliation: Division of Cardiothoracic Anesthesia, Department of Anesthesiology, Emory University School of Medicine, Atlanta, Georgia 30322

Treatment of bronchospasm with sympathomimetic drugs may lead to the development of life-threatening arrhythmias, especially under conditions of anesthesia, hypoxia, and hypercarbia. This study compared the arrhythmogenic potential of terbutaline (T) and epinephrine (E) administered intravenously to dogs anesthetized with halothane or pentobarbital under conditions of normal and hypoventilation.

METHODS. Twenty-five mongrel dogs (15±3 SD kg) were anesthetized as follows: Group I-12 dogs with 1.3% end-tidal (1.5 MAC) halothane and normal ventialtion (P_aO_2>100 torr, P_aCO_2 35-45 torr); Group II - 5 dogs with pentobarbital (30 mg/kg) and normal ventilation; Group III-8 dogs with pentobarbital (30mg/kg) and hypoventilation (P_aO_2<50 torr, P_aCO_2>70 torr). All dogs received pancuronium (0.1-0.2 mg/kg). Cannulae were inserted percutaneously in a femoral artery and foreleg vein. Lactated Ringers solution with 5% dextrose was infused (5-10cc/kg/hr). Body temperature was maintained at 37±1°C. Arterial PO_2, PCO_2, and pH were determined intermittently and base deficits ≥ 5mEq/L were corrected with sodium bicarbonate. Lead II of the ECG and arterial blood pressure (BP) were recorded continuously. Incremental doses of E(0.1-80µg/kg) and cumulative doses of T (1-1086µg/kg) were administered IV over a 1 min period. One-half the dogs in each group received E doses initially followed by T doses; the reverse was true for the other half. The ECG was examined for a minimum of 5 min after each dose for the presence of arrhythmias. Heart rate (HR) and BP were allowed to return to control levels following the administration of each dose of E. Because of the prolonged action of T, each dose was administered after an interval of 5 min between doses and the cumulative dose was recorded. The arrhythmogenic dose was that dose producing 10 or more ectopic beats during the 5 min period following drug administration. The next higher dose was administered until either the arrhythmogenic dose was defined or the maximum dose had been given. A 90 min recovery period occurred between the administration of T doses and the beginning of E administration. The inequality of numbers of dogs in each group is due to the fact that some dogs succumbed to arrhythmias from E or from hypotension from T.

RESULTS. All animals developed arrhythmias after E under all conditions. Only some animals in each group developed arrhythmias after T, and the arrhythmogenic doses were very much greater than for E (Table 1). Six of the 7 animals in the hypoventilated group developed severe hypotension and died following the largest doses of T; 3 died without developing arrhythmias. Both drugs produced dose-related hemodynamic changes. E resulted in elevations of diastolic and systolic BP and HR. T produced a greater increase in HR but a marked decrease in both systolic and diastolic BP (Table 2).

DISCUSSION. These data confirm the well-known arrhythmogenic actions of epinephrine. They demonstrate that under similar conditions terbutaline was a much less potent arrhyrhmogenic drug and that hypotension and tachycardia limited the maximum dose tolerated by the dog. To the extent that responses in dogs are comparable to those in man, the maximum tolerated dose of terbutaline is much greater than that usually required for therapy of bronchospasm in anesthetized patients.

TABLE 1
ARRHYTHMOGENIC EFFECTS OF SYMPATHOMIMETIC DRUGS

	Group I	Group II	Group III
Epinephrine			
No. of dogs developing arrhythmias	11/11	5/5	5/5
Arrhythmogenic dose (µg/kg ± SE)	3.8±0.7	24±11	40±11
Terbutaline			
No. of dogs developing arrhythmias	2/10	1/5	4/7*
Arrhythmogenic dose (µg/kg)	88;389	1086	231±87

*Three dogs died of hypotension without developing arrhythmias at a mean dose of 946 ± 72µg/kg.

TABLE 2
HEMODYNAMIC CHANGES (MEAN ± SE) AT THE ARRHYTHMOGENIC OR MAXIMUM ADMINISTERED DOSE

	Group I	Group II	Group III
Epinephrine-dose →	3.8±0.7	24±11	40±11
Heart Rate			
Control	127±17	174±20	152±13
After epi.	166±20**	212±28	194±12*
Systolic BP			
Control	101±4	132±10	182±16
After epi.	185±11**	266±30**	246±19
Diastolic BP			
Control	53±3	67±4	97±14
After epi.	121±9**	168±18**	184±12**
Terbutaline-dose →	915±183	968±80	537±154
Heart Rate			
Control	95±6	167±9	147±10
After terbut.	249±14**	261±8**	196±7
Systolic BP			
Control	112±7	156±10	179±9
After terbut.	81±5*	101±8*	67±6**
Diastolic BP			
Control	60±6	96±6	100±6
After terbut.	43±3*	54±2**	36±5**

*p<.05, **p<.01 compared to the control value.