Effects of Saffan on Cardiopulmonary Function in Healthy Cats

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ABSTRACT

The effects of saffan on cardiopulmonary function were evaluated in eight healthy adult cats. Measured values were cardiac output by thermodilution, heart rate by electrocardiogram, arterial blood gases, respiratory rate and systolic, diastolic and mean arterial blood pressures by arterial catheterization. Calculated values included cardiac index, stroke volume and systemic vascular resistance. Statistical analysis employed paired t-tests comparing pre saffan anesthetic induction and post saffan anesthetic parameters over a 120 minute time sequence. Thirty min after saffan induction, significant depression in cardiac output was evident while stroke volume was significantly depressed at 45 and 60 min, systolic blood pressure at 15 min and respiratory rate at 5, 10 and 15 min. No significant changes occurred in cardiac index, heart rate, arterial blood gases, diastolic and mean arterial blood pressure or systemic vascular resistance. It was concluded that saffan causes significant depression of cardiopulmonary function in normal adult cats.

Key words: Saffan, cardiac output, blood pressure, thermodilution, feline anesthesia.

RÉSUMÉ

Cette expérience consistait à évaluer les effets du saffan sur la fonction cardio-pulmonaire, chez huit chats adultes et en santé. On mesura le débit cardiaque, par la thermodilution; la fréquence cardiaque, par l'électrocardiogramme; les gaz sanguins artériels, la fréquence respiratoire, ainsi que les pressions sanguines systolique, diastolique et artérielle moyenne, par cathétérisme artériel. Le calcul des valeurs portait sur l'indice cardiaque, le débit systolique et la résistance vasculaire systémique. L'analyse statistique se fit au moyen de test-t appariés qui comparaient l'induction de l'anesthésie, avant l'injection de saffan, et les paramètres de l'anesthésie, durant les 120 minutes ultérieures à l'injection de saffan. Trente minutes après l'administration de saffan on constata une dépression significative du débit cardiaque, tandis que le débit systolique afficha une baisse appréciable, au bout de 45 et 60 minutes; la pression sanguine systolique, au bout de 15 minutes; le rhythme respiratoire, au bout de cinq, dix et 15 minutes. Aucun changement significatif ne se produisit dans l'indice cardiaque, la fréquence cardiaque, les gaz sanguins artériels, la pression sanguine diastolique et artérielle, ou la résistance vasculaire systémique. Les auteurs conclurent que le saffan cause une dépression significative de la fonction cardio-pulmonaire, chez les chats adultes et normaux.

Mots clés: saffan, débit cardiaque, pression sanguine, thermodilution, anesthésie féline.

INTRODUCTION

Alphaxalone-alphadolone (Saffan, Glaxovet, Toronto) is a steroid anesthetic agent marketed for use in cats as a sedative or general anesthetic. It has been widely used in humans where its cardiopulmonary effects have been well documented (1,2,3). Similar studies have been reported in cats (4,5,6,7). Cardiac output (CO), cardiac index (CI), stroke volume (SV) and systemic vascular resistance (SVR) however were not investigated in these reports. In healthy cats saffan has been shown to be a safe drug with a wide therapeutic margin and few serious side effects (8,9,10,11,12,13,14,15). Its cardiovascular effects are considered similar to or less depressive than those of thiopentone (3,16,17). Saffan anesthesia is characterized by rapid induction and recovery, good muscle relaxation and no cumulative effects with subsequent use of the drug (3,4,13,15,16). It can however, cause moderate hypotension, mild respiratory depression and histamine-like reactions (8,10,14,18). Hypotensive effects are considered by some authors to be mild to moderate and of short duration (4,5,6) while other reports state that hypotensive effects are significant and prolonged (7). In humans saffan is not considered a safe anesthetic for use in hypertensive or hypovolemic states (2).

The indices of CO, CI, SV and SVR should further characterize the effects of this drug on cardiac performance in the healthy adult cat.

MATERIALS AND METHODS

Eight healthy, mature cats (2.5 kg to 5.1 kg) of both sexes and mixed breeds were used. Each was judged to have a normal cardiovascular system as defined by history, physical examination, chest radiography and ECG. One day prior to the study, cats were anesthetized by facemask with 5% halothane in 100% O_2 at 5 L/min. They were then intubated and maintained on light halothane anesthesia. Thermodilution (Edwards Laboratories, Santa Ana, California) and arterial pressure catheters were placed in the left jugular vein and carotid artery respectively (19). Fluoroscopy verified positioning of the pulmonary artery thermistor and the right atrial injectate catheters. A 5-10% blood loss was common during the procedure. The skin wound was then closed and the neck bandaged for easy catheter access. Twenty-four hours later, the thermodilution catheter was connected

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Financial support given in part by the Canadian Veterinary Research Trust Fund.

Submitted June 4, 1986

to an Edwards Laboratory cardiac output computer. Two mL of 5% dextrose in water at room temperature was used as injectate. Measured CO was subsequently displayed by digital readout. Stroke volume, SVR and CI were calculated. The HR, ECG changes, and blood pressure (Tectronics, Beaverton, Oregon) were recorded. Respiratory rate and pattern were monitored visually. An arterial sample was taken for blood gas analysis (ABL3 Analyzer, Radiometer, Copenhagen, Denmark). These data served as the control. Values for CO, HR, arterial blood gases, RR, systolic, diastolic and mean arterial BP were recorded at control time 0 and at 5, 10, 15, 30, 45, 60, 90 and 120 min after saffan induction (12 mg/kg intravenously). Control values and the serially measured values were statistically analyzed using multiple paired t-tests comparing the control value to those values recorded following saffan administration. Comparison was made only to changes in the cat under study. Each cat therefore served as its own control. Significant changes ($p < 0.0063$) were addressed.

RESULTS

The duration of anesthesia was 30-45 min in most cats.

Respiration was significantly depressed at 5, 10 and 15 min postanesthetic injection (Fig. 1, Table III). Respiratory rate slowed significantly. One cat became apneic for five minutes and required intermittent positive pressure ventilation. This cat returned to spontaneous ventilation. Blood gas data from this animal was not used in the analysis.

Blood gas changes were not statistically significant, although a slight rise in pCO_2 occurred during the first 15 min and corresponded to the observed depression of RR (Table III). The values for pO_2 were also not statistically altered although a slight reduction was observed during the first 30 min. These values remained within a clinically acceptable range (mean > 85 mmHg).

Cardiac output fell significantly below control values only at 30 min following saffan induction (Fig. 1, Table I). The fall in CO was associated with a fall in SV. Although HR increased slightly, it did not do so to a significant degree. Decreased CO was noted to develop within the first 5 min of the study and to persist throughout the entire experiment. This is in contrast to results reported by others. Although a statistically significant fall in SV did not occur until 45 and 60 min, depression in SV was apparent 5 min after induction and continued to the end of the study (Fig. 1, Table I).

Systolic arterial B.P. was significantly depressed 15 min following induction (Fig. 1, Table II). Although a fall in mean, diastolic and systolic arterial BP was also noted in all cases throughout the study period, these changes were not statistically significant. No significant changes in SVR were observed (Table II). Cardiac index changes were not statistically significant in this study (Table I).

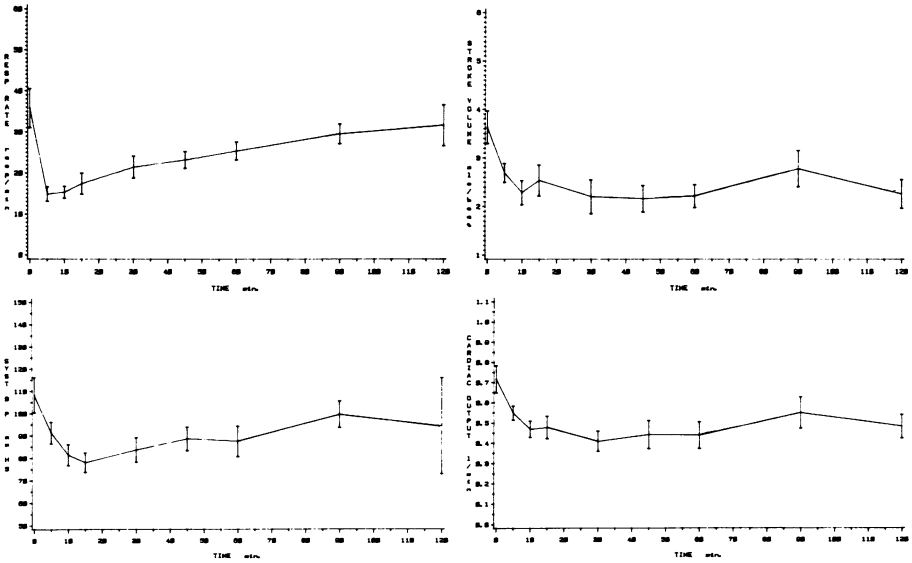

Fig. 1. Parameters of cardiopulmonary function versus time in healthy adult cats under saffan anesthesia. Standard error bars are shown.

TABLE I. Parameters of Cardiac Function of Cats Under Saffan Anesthesia

Time (min)	Cardiac Output (L/min)		Cardiac Index (mL/min/kg)		Stroke Volume (mL/beat)		Heart Rate (beats/min)	
	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.
0	0.72	0.190	200.00	62.85	3.63	0.95	198	24
5	0.55	0.092	156.57	43.32	2.69	0.51	207	10
10	0.47	0.108	134.57	44.64	2.29	0.66	204	21
15	0.48	0.157	130.38	40.96	2.54	0.91	192	27
30	0.41	0.132	116.86	40.69	2.20	0.93	204	43
45	0.44	0.185	124.71	43.51	2.16	0.72	210	45
60	0.44	0.175	126.43	50.14	2.21	0.62	202	49
90	0.55	0.207	161.71	71.21	2.78	0.99	213	45
120	0.48	0.103	122.33	8.96	2.27	0.51	215	31

TABLE II. Parameters of Cardiac Function of Cats Under Saffan Anesthesia

Time	Syst BP mmHg		Dia BP (mmHg)		Mean BP mmHg		Systemic Vascular Resistance dynes sec cm^{-5}	
	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.
0	108.25	22.34	79.38	24.68	92.25	22.78	11127.13	4655.79
5	91.29	12.80	63.43	6.24	75.71	5.09	11234.33	2453.91
10	81.43	12.39	54.57	10.63	70.00	4.82	13376.20	3465.27
15	78.13	12.30	50.00	14.62	63.63	13.50	11854.63	5074.82
30	83.75	15.36	54.13	16.08	65.25	15.43	13770.43	6016.13
45	88.63	14.96	55.50	13.04	69.25	12.48	14053.57	4710.56
60	87.50	19.30	58.63	17.28	69.63	17.09	13766.29	3726.92
90	99.63	16.93	69.75	14.15	81.25	14.61	13102.57	5405.63
120	94.50	30.41	71.00	26.89	85.00	23.07	14628.67	5029.31

TABLE III. Parameters of Respiratory Function of Cats Under Saffan Anesthesia

Time (min)	PO_2 mmHg		PCO_2 mmHg		PH		Resp. Rate breaths/min	
	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.
0	107.77	9.04	27.95	2.44	7.41	0.04	36	14
5	89.36	16.73	31.37	4.22	7.34	0.10	15	5
10	88.77	15.13	32.62	3.78	7.32	0.08	15	4
15	90.02	16.93	33.64	4.76	7.33	0.09	17	8
30	97.53	8.34	30.69	6.76	7.31	0.13	22	8
45	102.37	13.13	25.32	6.58	7.39	0.07	23	6
60	101.31	14.12	26.24	5.93	7.37	0.07	26	7
90	104.98	21.31	22.23	3.65	7.39	0.10	30	7
120	110.10	0.42	22.45	5.02	7.39	0.01	32	9

DISCUSSION

In humans saffan anesthesia is characterized by a fall in SVR, followed by a fall in arterial BP, central venous pressure and SV. Cardiac output remains unchanged or rises slightly due to a corresponding increase in HR. In cats, hypotension is related to peripheral vasodilation (20). In this study CO was significantly decreased (Fig. 1). Thirty minutes following saffan anesthesia it had fallen to 57% of control values. At this time SV was also decreased and HR had increased only slightly. The reduction in CO was a function of the decline in SV. A fall in SV following saffan anesthesia has been documented in humans (1). The HR however, has been observed to increase subsequent to the fall in SVR. The increases in heart rates were small or transient (4,5,6,7). In this study the maximal increase in HR (8%) was not sufficient to maintain CO at preinduction levels. Although resting heart rates were elevated at time 0 they were still within a normally accepted range. A further increase in rate would not have provided any rise in CO because of the inability to raise preload.

Stroke volume is a reflection of preload, afterload and contractility. In humans, saffan causes a fall in SVR followed by a subsequent fall in SV. Central venous pressure remains constant or falls. Further, it has been shown that saffan has a small negative inotropic effect (1,3,4,5). Systemic vascular resistance did not change significantly in this study and since SVR is a measure of mean arterial pressure divided by CO it was concluded that mean arterial pressure and CO fell proportionately (20).

Mean arterial BP falls during saffan anesthesia (1,2). In this study, arterial systolic BP did decrease significantly 15 minutes into the study. This was equivalent to a 28% decline from control values (Fig. 1). A sustained fall in systolic BP in cats has been previously noted (4). Middleton stated that saffan induces profound and sustained hypotension at a dose of 9 mg/kg IV. Saffan has also been associated with as much as a 60% decrease in arterial blood pressure, compared to control values (7). However, other studies have stated that the hypotensive effects of saffan are mild and transient even at a dose of 15 mg/kg IM (4,6). In this study mean arterial BP fell no more than 31% of control values. Mean BP did, however, remain below control values throughout the experimental period.

In contrast to results of investigators who noted hyperventilation with saffan anesthesia, this study documented a depressant effect (6,7,12). Hyperventilation has been attributed to the hypotension which in this study did not appear sufficient to trigger the anticipated increased respiratory rate (7). Hyperventilation has also been attributed to central nervous system stimulation (1). Despite the reduction in respiratory rate there were no significant blood gas changes noted, indicating that there may have been a compensatory increase in tidal volume. A short period of apnea has been documented in humans and was noted in one of our cats (1). Further, in contrast to previous studies which documented only transient effects on arterial BP, SV and RR, this study demonstrated a prolonged depressant effect of the drug on CO, SV, RR and arterial BP (6,16,17). Dose may have been a factor. The 12 mg/kg IV used in this study was different than that used by other investigators who studied the drug at a dose of 15 mg/kg IM (4) and 9 mg/kg IV (7,18).

It can be concluded that saffan, at a dose of 12 mg/kg IV, does have significant cardiovascular depressant effects in the normal adult cat. It may also cause apnea. It would therefore not be a recommended anesthetic choice at this dose in the cat with compromised cardiovascular or pulmonary function. However, even at this dose all cats survived, demonstrating a wide safety margin (16).

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