Hemodynamic and anesthetic effects of etomidate infusion in medetomidine-premedicated dogs

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Summary

Hemodynamic and analgesic effects of medetomidine (15 μg/kg of body weight, IM) and etomidate (0.5 mg/kg, IV, loading dose; 50 μg/kg/min, constant infusion) were evaluated in 6 healthy adult Beagles. Instrumentation was performed during isoflurane/oxygen-maintained anesthesia. Before initiation of the study, isoflurane was allowed to reach end-tidal concentration ≤ 0.5%, when baseline measurements were recorded. Medetomidine and atropine (0.044 mg/kg) were given IM after recording of baseline values. Ten minutes later, the loading dose of etomidate was given IM, and constant infusion was begun and continued for 60 minutes. Oxygen was administered via endotracheal tube throughout the study. Analgesia was evaluated by use of the standard tail clamp technique and a direct-current nerve stimulator.

Sinoatrial and atrial-ventricular blocks occurred in 4 of 6 dogs within 2 minutes after administration of a medetomidine-atropine combination, but disappeared within 8 minutes. Apnea did not occur after administration of the etomidate loading dose. Analgesia was complete and consistent throughout 60 minutes of etomidate infusion. Medetomidine significantly ($P < 0.05$) increased systemic vascular resistance and decreased cardiac output. Etomidate infusion caused a decrease in respiratory function, but minimal changes in hemodynamic values. Time from termination of etomidate infusion to extubation, sternal recumbency, standing normally, and walking normally were 17.3 ± 9.4, 43.8 ± 14.2, 53.7 ± 11.9, and 61.0 ± 10.9 minutes, respectively. All recoveries were smooth and unremarkable. We concluded that this anesthetic drug combination, at the dosages used, is a safe technique in healthy Beagles.

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Medetomidine[a] is a selective α_2-adrenergic receptor agonist that induces sedation, analgesia, and muscular relaxation in dogs.[1-3] It has been used in conjunction with hypnotic drugs, such as propofol, to provide short-term general anesthesia in dogs.[4,5,b]

Etomidate[c] is a short-acting, nonwater soluble, nonbarbiturate IV administered hypnotic anesthetic[6,7] with poor analgesic properties. It characteristically maintains hemodynamic stability with minimal respiratory depression and has a wide margin of safety. Rapid recovery follows either a single bolus or continuous infusion of etomidate.[8] It has been used for induction of anesthesia in dogs.[9,10] The induction dosage reported in nonpremedicated and premedicated dogs varies from 0.9 ± 0.3 to 1.3 ± 0.2 mg/kg of body weight, IV.[10] Use of etomidate for maintenance of general anesthesia for surgeries of a painful nature requires supplementation with analgesic and muscular relaxant drugs.

To the author's knowledge, the hemodynamic effect of medetomidine in combination with etomidate infusion has not been reported. The purpose of the study reported here was to assess the hemodynamic effects of medetomidine, when combined with an induction dose of etomidate, followed by constant infusion of etomidate. In a preliminary study, dogs receiving medetomidine (30 μg/kg, IM) followed by etomidate (1 mg/kg, IV) and loading dose infusion (100 μg/kg/min, IV) became apneic after the etomidate induction dose. Respiratory depression was accompanied by cardiovascular depression during constant infusion. However, 2 dogs without medetomidine premedication, then were given a bolus of etomidate (2 mg/kg, IV) followed by constant infusion (110 μg/kg/min), had only minimal analgesia, but respiratory depression was a constant characteristic response. On the basis of this information, we chose to use medetomidine dosage of 15 μg/kg, IM, and etomidate dosage of 0.5 mg/kg, IV, for anesthesia induction. Etomidate constant infusion was maintained at the rate of 50 μg/kg/min.

Materials and Methods

Dogs—Six healthy purebred Beagles, 3 males and 3 females, weighing from 8.8 to 10.9 kg were studied.

[a] Domitor, Orion Corp, Farmos Group Ltd, Finland.

[b] Thurmon JC, Ko JCH, Benson GJ, et al. Clinical Assessment of a combination of medetomidine and propofol as anesthetics in dogs (abstr), in *Proceedings*. Vet Midwest Anesth Conf, May 23, 1992.

[c] Amidate, Abbott Laboratories, North Chicago, Ill.

Dogs were housed in the AALAC-approved facilities and were fed a standard commercial diet.

Instrumentation—Anesthesia was induced and maintained by administration of isoflurane in O_2 via nose cone and a cuffed endotracheal tube, respectively. Dogs were positioned in left lateral recumbency for instrumentation. A 20-gauge over-the-needle catheter[d] was placed percutaneously into a femoral artery for measurement of blood pressure (BP) by use of a pressure transducer (calibrated with a mercury manometer)[e] and was recorded on a physiograph.[f] The midline of the sternum was used as the reference point for transducer position. Blood samples were collected anaerobically from this arterial catheter for determination of blood gas tensions (Pa_{CO_2} and Pa_{O_2}) and acid-base status (pHa and base excess).[g] Using aseptic technique, the right jugular vein was cannulated with a catheter introducer,[h] through which a thermodilution catheter[i] was passed into the pulmonary artery for determination of cardiac output (CO).[j] Final resting positions of the pulmonary artery catheter tip and injection ports (located in right atrium) were determined by observing intravascular pressures and characteristic wave forms on the recorder. Limb lead-II of the ECG was monitored continuously. After instrumentation, dogs were allowed to breath 100% oxygen via an endotracheal tube. The oxygen float rate was set at 3 L/min throughout the anesthetic period via a circle system.[k]

Measurements—End-tidal isoflurane and CO_2 concentrations were measured by use of a medical gas analyzer.[l] Gas samples were drawn from a catheter, the tip of which was positioned in the trachea near the level of the carina. Isoflurane administration was discontinued when instrumentation was completed. The dog was allowed to recover from anesthesia until end-tidal isoflurane concentration reached ≤ 0.5% or when the dog moved spontaneously.

Baseline values were recorded for the following variables: heart rate (HR), respiratory rate (RR), CO, BP (systolic, diastolic, and mean), pulmonary arterial blood pressure (PAP), pulmonary capillary wedge pressure (PCWP), central venous pressure (CVP), core body temperature recorded from the thermodilution catheter thermistor, Pa_{CO_2}, Pa_{O_2}, pHa and intensity of analgesia. Analgesia was evaluated, using a constant current nerve stimulator[m] followed by a standard tail clamp method.[11] The clamp was applied at an area (2nd to 3rd coccygeal vertebrae) where the hair had been clipped from the skin. The clamp was locked to the first ratchet to produce a repeatable force and was left in place for 30 seconds or until the dog responded. Using the nerve stimulator, 2 one-inch needles were placed subcutaneously on either side of the tail at the junction of the 5th and 6th coccygeal vertebrae. Serial stimulations ranging from 10 to 100 V in 10-V steps were applied until gross purposeful movement or 100 V was reached. The nerve stimulator has a built-in constant current device that delivers a known amount of current as voltage changes. Gross purposeful movements associated with the electrical stimulus were considered lack of analgesia. Analgesia was evaluated immediately after etomidate administration and continued at 10-minute intervals until termination of etomidate infusion. Analgesic evaluations were always conducted after all readings that could be influenced by stimulation (ie, sedative score, HR, RR, and BP) had been recorded.

Values were calculated for cardiac index (CO/body surface area in m^2),[12] systemic vascular resistance (SVR; {mean BP − CVP}/CO × 80; dynes·s/cm^5), pulmonary vascular resistance (PVR; {PAP − PCWP}/CO × 80; dynes·s/cm^5), rate pressure product (HR × systolic BP × 10^{-2}; beats/min × mm of Hg), stroke volume (SV; CO × 1,000/HR; ml/beat), stroke index (SI; SV/body surface area in m^2; ml/beat/m^2), left ventricular stroke work index ({1.36 × mean BP − PCWP} × SI/100; g·m/m^2), and right ventricular stroke work index ({1.36 × PAP − CVP} × SI/100; g·m·/m^2).[13]

Immediately after baseline values (time 0) were recorded, medetomidine (15 μg/kg) and atropine (0.044 mg/kg) were administered IM. Variables were recorded at 5 and 10 minutes after administration of the medetomidine-atropine combination. Etomidate was administered (0.5 mg/kg) IV as a single bolus, and constant infusion was immediately begun at a rate of 50 μg/kg/min and continued for 60 minutes.

Hemodynamic and analgesic data were collected 5 minutes after etomidate administration and thereafter at 10-minute intervals. Variables were also recorded 5 minutes after termination of etomidate infusion. At the end of study, catheters were removed and dogs were allowed to recover.

Analysis of data—Data were analyzed by use of ANOVA for repeated measures. When significant F values were found, a least-significant different test was performed to determine differences among means. Probability value of 5% was considered significant. All values are reported as mean ± SEM.

Results

Sinoatrial and atrial-ventricular block occurred in 4 of 6 dogs within 2 minutes of medetomidine-atropine administration, but disappeared within 8 minutes. Heart rate, mean arterial BP, CVP, rate pressure product, right ventricular stroke work index, left ventricular stroke work index, and Pa_{O_2} did not change after subsequent etomidate administration (Tables 1–3).

Cardiac output, CI, SV, and RR decreased 5 minutes after medetomidine-atropine administration, and

[d] Angiocath, Vascular Access, Becton, Dickinson & Co, Sandy, Utah.
[e] P23ID Transducer, Stathan Medical Instrument, Gould Inc, Oxnard, Calif.
[f] Brusch 260, Gould Inc, Oxnard, Calif.
[g] 158 ph/blood gas analyzer, Corning Medical & Scientific, Medfield, Mass.
[h] Desilet-Hoffman introducer set, A cook Group Co, Bloomington, Ind.
[i] Swan-Ganz flow-directed thermodilution catheter, American Edwards Laboratories, Santa Ana, Calif.
[j] Model 9520A cardiac output computer, American Edward Laboratories, Irvine, Calif.
[k] Narcovet, Anesthesia Machine, North American Drager, Telford, Pa.
[l] Datex, 254 Airway Gas Monitor, Instrumentaroum Corp, Helsinki, Finland.
[m] S88 stimulator, Grass Instruments Quincy, Mass.

Table 1—Effects of medetomidine-atropine combination and etomidate infusion on recorded hemodynamic values in dogs (n = 6)

Time (min)	MAP (mm of Hg)	CO (L/min)	PCWP (mm of Hg)	CVP (mm of Hg)	PAP (mm of Hg)	HR (beats/min)	SV (ml/min)
0	92.0 ± 4.6	1.8 ± 0.05[b]	4.9 ± 0.8	1.8 ± 0.3	10.8 ± 0.8[a]	105.5 ± 2.5	16.9 ± 0.7[b]
5	154.7 ± 23.7	0.7 ± 0.04[b]	12.8 ± 2.8[a]	5.4 ± 1.5	20.1 ± 4.2[a]	82.0 ± 24.7	11.8 ± 2.31[b]
10	179.3 ± 31.6	0.8 ± 0.07[b]	23.2 ± 4.1[a]	5.5 ± 1.6	29.8 ± 3.8[a]	133.0 ± 30.1	8.8 ± 2.70[b]
15	167.2 ± 18.9	0.9 ± 0.10[b]	21.0 ± 1.9[a]	6.5 ± 1.3	28.5 ± 2.0[a]	139.0 ± 25.8	7.4 ± 1.44[b]
20	179.0 ± 17.5	1.0 ± 0.08[b]	21.3 ± 3.6[a]	6.5 ± 1.4	26.0 ± 3.9[a]	137.0 ± 21.9	8.0 ± 1.53[b]
30	173.3 ± 17.8	1.0 ± 0.07[b]	17.7 ± 3.3[a]	4.6 ± 1.4	20.8 ± 3.1[a]	139.5 ± 11.6	7.2 ± 0.28[b]
40	173.3 ± 18.3	1.0 ± 0.07[b]	18.8 ± 2.8[a]	3.3 ± 1.5	21.5 ± 2.8[a]	124.0 ± 7.3	7.8 ± 0.64[b]
50	158.0 ± 17.3	1.0 ± 0.04[b]	16.3 ± 2.0[a]	2.9 ± 1.6	18.6 ± 2.2[a]	112.5 ± 7.5	9.0 ± 0.72[b]
60	152.5 ± 17.3	1.0 ± 0.07[b]	13.7 ± 1.9[a]	2.7 ± 1.3	17.3 ± 2.5[a]	101.7 ± 5.7	10.1 ± 0.76[b]
70	152.6 ± 17.3	1.0 ± 0.07[b]	13.5 ± 2.0[a]	2.0 ± 1.3	17.5 ± 1.4[a]	101.0 ± 6.5	10.4 ± 1.03[b]
75	156.6 ± 16.3	1.0 ± 0.08[b]	12.7 ± 2.2[a]	3.0 ± 1.2	16.7 ± 1.8[a]	98.0 ± 4.3	10.1 ± 1.00[b]

[a] Significant ($P < 0.05$) increase from baseline. [b] Significant ($P < 0.05$) decrease from baseline.
MAP = mean arterial pressure; CO = cardiac output; PCWP = pulmonary capillary wedge pressure; CVP = central venous pressure; PAP = pulmonary arterial pressure; HR = heart rate; SV = stroke volume.
Data are expressed as mean ± SEM.

Table 2—Effects of medetomidine-atropine combination and etomidate infusion on derived hemodynamic values in dogs (n = 6)

Time (min)	SI (ml/beat/m^2)	CL (L/min/m^2)	SVR (dynes · s/cm^5)	PVR (dynes · s/cm^5)	RPP (beats/min · mm of Hg × 10^{-2})	LVSWI (g · m/m^2)	RVSWI (g · m/m^2)
0	36.2 ± 1.0	3.81 ± 0.12	4,068.1 ± 189.7	282.2 ± 64.2	13,774.0 ± 727.7	43.5 ± 2.4	4.6 ± 0.3
5	25.3 ± 5.2[b]	1.53 ± 0.09[b]	15,858.9 ± 2,876.2[a]	819.2 ± 192.4[a]	18,413.0 ± 7,651.8	46.3 ± 9.2	3.9 ± 0.7
10	18.7 ± 5.4[b]	1.69 ± 0.14[b]	18,513.9 ± 3,915.5[a]	642.2 ± 338.6[a]	32,537.0 ± 9,398.6	36.2 ± 7.9	5.4 ± 0.9
15	15.7 ± 2.8[b]	1.86 ± 0.19[b]	15,911.4 ± 2,478.2[a]	672.6 ± 175.8[a]	26,893.0 ± 6,472.6	30.9 ± 4.9	4.6 ± 0.3
20	17.2 ± 3.0[b]	2.06 ± 0.13[b]	14,974.6 ± 1,982.9[a]	398.8 ± 84.1	30,286.0 ± 5,711.9	37.7 ± 6.9	5.3 ± 1.6
30	15.5 ± 0.7[b]	2.13 ± 01.4[b]	13,943.8 ± 1,729.9[a]	269.7 ± 83.2	29,427.0 ± 3,973.8	34.3 ± 4.3	3.7 ± 0.6
40	16.7 ± 1.2[b]	2.05 ± 0.14[b]	14,710.3 ± 2,145.0[a]	222.7 ± 78.0	25,987.0 ± 2,964.8	36.9 ± 5.4	4.4 ± 0.7
50	19.4 ± 1.6[b]	2.13 ± 0.09[b]	12,363.1 ± 1,053.3[a]	180.8 ± 56.5	21,476.0 ± 2,371.9	39.8 ± 6.1	4.3 ± 0.5
60	20.1 ± 1.1[b]	3.75 ± 1.62[b]	11,706.5 ± 968.5[a]	269.9 ± 121.0	18,986.5 ± 2,442.9	39.2 ± 4.7	4.1 ± 0.5
70	22.4 ± 2.3[b]	2.19 ± 0.15[b]	11,679.1 ± 1,020.6[a]	298.7 ± 94.1	199,434.0 ± 2,564.6	44.9 ± 7.0	4.9 ± 0.5
75	21.7 ± 1.9[b]	2.09 ± 0.16[b]	12,512.0 ± 990.9[a]	328.0 ± 121.2	18,720.0 ± 1,887.4	45.5 ± 7.3	4.3 ± 0.5

[a] Significant ($P < 0.05$) increase from baseline. [b] Significant ($P < 0.05$) decrease from baseline.
SI = stroke index; CI = cardiac index; SVR = systemic vascular resistance; PVR = pulmonary vascular resistance; RPP = rate pressure product; LVSWI = left ventricular stroke work index; RVSWI = right ventricular stroke work index.
See Table 1 for key.

Table 3—Effects of medetomidine-atropine combination and etomidate infusion on respiratory rate and arterial blood gas values in dogs (n = 6)

Time (min)	RR (breaths/min)	pHa	Pa_{CO_2} (mm of Hg)	Pa_{O_2} (mm of Hg)	Temperature (C)	Analgesia (V)	Tail clamp (response/no response)
0	35.8 ± 5.5	7.28 ± 0.02	41.1 ± 1.6	533.5 ± 19.6	37.7 ± 0.1	...	...
5	19.5 ± 5.8[b]	7.30 ± 0.02	37.4 ± 2.2	519.0 ± 14.5	37.7 ± 0.1	...	...
10	17.8 ± 5.7[b]	7.30 ± 0.02	40.8 ± 1.8	518.9 ± 18.4	37.5 ± 0.1	...	...
15	14.7 ± 2.9[b]	7.21 ± 0.02[b]	40.5 ± 2.6[a]	525.4 ± 14.3	37.4 ± 0.1[b]	100.0 ± 0.0	0/6
20	15.8 ± 4.5[b]	7.22 ± 0.02[b]	46.8 ± 3.7[a]	518.2 ± 22.7	37.3 ± 0.1[b]	100.0 ± 0.0	0/6
30	13.8 ± 3.9[b]	7.22 ± 0.02[b]	47.8 ± 2.3[a]	516.3 ± 15.5	37.3 ± 0.1[b]	100.0 ± 0.0	0/6
40	12.8 ± 4.2[b]	7.22 ± 0.02[b]	47.6 ± 2.5[a]	515.4 ± 16.2	37.2 ± 0.1[b]	100.0 ± 0.0	0/6
50	13.0 ± 3.9[b]	7.20 ± 0.02[b]	54.0 ± 4.2[a]	519.3 ± 22.1	37.0 ± 0.1[b]	100.0 ± 0.0	0/6
60	14.0 ± 3.9[b]	7.20 ± 0.02[b]	53.2 ± 4.9[a]	514.2 ± 12.3	37.0 ± 0.1[b]	100.0 ± 0.0	0/6
70	16.8 ± 3.5[b]	7.21 ± 0.03[b]	51.2 ± 5.2[a]	500.5 ± 15.9	37.0 ± 0.2[b]	100.0 ± 0.0	0/6
75	20.8 ± 3.5[b]	7.23 ± 0.02[b]	46.9 ± 3.3[a]	502.4 ± 14.0	36.7 ± 0.2[b]	...	...

[a] Significant ($P < 0.05$) increase from baseline. [b] Significant ($P < 0.05$) decrease from baseline.
RR = respiratory rate; Temperature = core body temperature; Tail clamp = total No. of dogs responded.
See Table 1 for key.

remained below the baseline values during etomidate administration (Tables 1–3). Pulmonary capillary wedge pressure, PAP, and SVR were increased 5 minutes after medetomidine-atropine administration and remained above baseline values during etomidate administration (Tables 1 and 2).

Arterial blood pH and core body temperature decreased, and Pa_{CO_2} increased during etomidate administration (Table 3). Induction dose of etomidate did not cause apnea. Time from termination of etomidate infusion to extubation, sternal recumbency, standing normally, and walking normally were 17.3 ± 9.4, 43.8 ± 14.2, 53.7 ± 11.9, and 61.0 ± 10.9 minutes, respectively. None of the 6 dogs responded to either electrical stimulation (100 V) or the tail clamp throughout the 60 minutes of etomidate infusion. All dogs recovered from anesthesia smoothly and without complications.

Discussion

Studies[14-16] have indicated that dosage of 20 to 40 μg/kg of medetomidine/kg induces bradycardia accompanied by second-degree atrioventricular block in dogs. Bradycardia with HR as low as 30 to 40 beats/min has been reported.[14-16] In our study, medetomidine (15 μg/kg) administered IM together with atropine (0.044 mg/kg) also resulted in bradycardia (55.4 ± 10.5 beats/min) characterized by the development of sinoatrial and atrioventricular block within 2 minutes of its administration in 4 of the 6 dogs. The HR had returned to 82 ± 24.7 beats/min at 5 minutes, however, and remained near baseline thereafter (Table 1). In another study,[5] medetomidine (30 μg/kg, IM) with atropine (0.044 mg/kg, IM) also induced bradycardia (50 ± 5.4 beats/min) and similar dysrhythmias within 2 minutes of drug administration. Medetomidine-induced bradycardia and dysrhythmia also developed rapidly (within minutes) after IM administration of a lower dose. This observation is similar to that of other reports where bradycardia and atrioventricular block developed within seconds to minutes after medetomidine administration.[14-16] Coadministration of atropine did not prevent these dysrhythmias initially, but appeared to have alleviated the bradycardia action within 5 minutes. Previous studies[14-16] have indicated that medetomidine-induced bradycardia persisted for several hours. In our study, use of atropine had effectively increased HR by 10 minutes after medetomidine-atropine administration (Table 1). It would seem that, when bradycardia, atrioventricular block, or both could possibly be a problem, administration of an anticholinergic drug prior to medetomidine injection should be considered.

Vickery et al[17] reported that CO in halothane-anesthetized dogs receiving 10 μg of medetomidine/kg decreased in conjunction with an increase in SVR. Those authors concluded that the decrease in CO after medetomidine administration was attributable to a decrease in HR and an increase in afterload, but was also accompanied by a decrease in myocardial oxygen requirement. In this study, medetomidine (15 μg/kg, IM) was associated with acute cardiovascular changes, similar to those observed after a 30 μg/kg dose[5] was give. The changes included decrease in CO and increase in PCWP and SVR.

Decrease in SV was responsible for the decrease in CO. Heart rate was unchanged at 5 and 10 minutes after medetomidine-atropine administration. Stroke volume is commonly determined by 3 major factors: preload, afterload, and contractility.[18]

Decrease in CO, together with increase in PCWP and SVR (Tables 1 and 2), indicate that the decrease in CO was attributable, in large part, to an increase in afterload, rather than a decrease in preload. Medetomidine-induced increases in SVR by stimulation of an α_2-adrenoceptor located in vascular smooth muscle.[17] In a medetomidine-propofol study,[5] the medetomidine-induced SVR appears to have been alleviated by the vasodilating effect of propofol within 5 minutes after IV administration. In this study, etomidate did not decrease medetomidine-induced increases in SVR.

Systemic vascular resistance remained increased and CO decreased during the entire study period. Etomidate reportedly has minimal hemodynamic altering actions. However, RR decreased after medetomidine administration. The RR decrease did not change pHa or Pa_{CO_2} however (Table 3). Similar results have been reported for use of a propofol-medetomidine (30 μg/kg, IM) combination in dogs.[5] Transient apnea has been reported to follow etomidate injection.[10] In our preliminary trials, the 2 dogs receiving bolus of etomidate (2 mg/kg, IV) followed by constant infusion (110 μg/kg/min) became apneic for approximately 2 minutes, and Pa_{CO_2} reached a value of 64 mm of Hg during the etomidate infusion period. In this study, etomidate (0.5 mg/kg), given IV 10 minutes after medetomidine (15 μg/kg, IM) did not cause apnea. However, after the loading dose and initiation of etomidate infusion, pHa decreased and Pa_{CO_2} remained increased until the end of study. Thus, the combination of medetomidine and etomidate caused noticeable depression of minute ventilation in our dogs.

Analgesia was considered adequate after etomidate loading and during the 60-minute infusion period. All dogs accepted 100 V and the tail clamp test without gross purposeful movement. On the basis of the results of the analgesia test, etomidate infusion in medetomidine-premedicated dogs should be suitable for minor surgery. Although core body temperature decreased, it remained within acceptable range throughout the study.

Although etomidate administration can cause pain, excitement, myoclonus, and vomiting during induction, these side effects can be minimized or eliminated. Diazepam, acetylpromazine, or morphine has been successfully used to prevent the side effects.[10] We did not observe any of these effects during induction or recovery. This may be attributed to premedication with medetomidine and atropine. In preliminary trials, myoclonus developed in 2 of the dogs receiving etomidate (2 mg/kg, IV) that were not premedicated with medetomidine-atropine combination. Vomiting and excitement also were noticed in these 2 dogs during the recovery period. In contrast, when the etomidate induction dose was decreased, recovery was smooth and unremarkable in medetomidine-atropine-premedicated dogs. After termination of etomidate infusion, dogs were extubated at mean time of 17.3 ± 9.4 minutes and were able to walk unassisted at mean time of 61.0 ± 10.9 minutes. This

suggests a low rate of drug accumulation, as characterized by minimal hangover from etomidate infusion.

The only side effect that we observed during this study was acute hemolysis after etomidate infusion. The acute hemolysis induced by etomidate has been further studied elsewhere.[19,20] It was concluded that etomidate in 35 volume percent propylene glycol preparation (etomidate-PG) caused acute hemolysis in dogs in vivo and in vitro. The mechanism of etomidate-PG-induced acute hemolysis in dogs[19] and human beings[20] is thought to be attributable to the extremely nonphysiologic osmolality of etomidate-PG. The clinical significance of this amount of hemolysis is not clear at this time and, thus, requires further study.

On the basis of hemodynamic and analgesic results of this study, healthy dogs premedicated with medetomidine at dosage of 15 μg/kg, IM, and having anesthesia loading lose induced with etomidate (0.5 mg/kg), followed by infusion (50 μg/kg/min), are subjected to adequate and safe anesthesia.

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