THE EFFECTS OF ETOMIDATE ON ARTERIAL PRESSURE, PULSE RATE AND PREGANGLIONIC SYMPATHETIC ACTIVITY IN CATS

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ETOMIDATE is a new short-acting non-barbiturate intravenous anaesthetic. It is water soluble and rapidly metabolized in the liver.¹ It has some cardiovascular actions similar to those found with short acting barbiturates,² althesin³ and propanidid⁴ in that it produces hypotension and tachycardia, but apparently to a lesser degree.⁵ Since no study has been made on the effect of etomidate on sympathetic nervous activity, we have done a study using the same technique as was used in the study of the other intravenous anaesthetics mentioned above.

METHOD AND MATERIAL

Ten cats were used in the experiment. They were studied under a basal anaesthesia of 50 per cent nitrous oxide in oxygen with decamethonium used for muscle relaxation. Respiration was controlled with a respirator. End-tidal carbon dioxide was measured by a capnograph and kept at constant level. Metabolic acidosis, if occurring, was corrected with intravenous sodium bicarbonate. Detailed description of the surgical preparation has been reported elsewhere.²

Sympathetic nervous activity was measured from teased strands of the left cervical sympathetic trunk. Arterial pressure was measured from a canula in a femoral artery. The following parameters were recorded on a Grass Polygraph: Arterial pressure, mean arterial pressure, end-tidal carbon dioxide, sympathetic nervous activity in impulses per second (imps/sec), and pulse rate measured by a tachograph triggered by the pulse wave.

Five animals were studied in a normal state with only the cervical sympathetic trunk sectioned. Five animals were studied in a baroreceptor-denervated state with all barostatic nerves and both vagi surgically sectioned.

Etomidate was administered as a bolus injection of 0.8 mg/kg, a dose selected in a few pilot studies as sufficient to produce a moderate decline in arterial pressure. Information about anaesthetic doses for etomidate required in cats were unavailable at the time of the study.

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EFFECTS OF ETOMIDATE ON SYMPATHETIC NERVOUS ACTIVITY ARTERIAL PRESSURE AND PULSE RATE IN CATS.

FIGURE 1. Effects of etomidate on sympathetic nervous activity, mean arterial pressure, and pulse rate in normal and baroreceptor-denervated cats (Table I in graphic form). High and low values were invariably reached within the first minute after injection of etomidate.

RESULTS

Normal Animals

The response of sympathetic nervous activity, mean arterial pressure, and pulse rate to etomidate is shown in Figures 1 and 2, and in Table I. After injection of etomidate in normal animals a marked decline was noted in sympathetic activity from 48 ± 7 to 4 ± 2 imps/sec ($p < 0.01$). It took 20 minutes for sympathetic activity to return to a level not significantly different from the initial level. Mean arterial blood pressure declined from 128 ± 7 to 108 ± 8 torr ($p < 0.05$), but returned to the initial level within one minute in spite of a markedly depressed sympathetic tone.

Pulse rate increased from 182 ± 11 to 214 ± 14 beats per minute ($p < 0.05$), but returned to the initial level within two minutes.

Denervated Animals

The response in sympathetic tone evoked by etomidate in denervated animals was similar to that found in normal animals. Sympathetic tone declined from 59 ± 8 imps/sec to 5 ± 2 imps/sec and recovered in 20 minutes. Mean arterial pressure fell significantly more than was observed in normal animals from 127 ± 16 to 67 ± 17 torr ($p < 0.01$). Based on a percentage level denervated animals also showed a significantly greater depression in arterial pressure than was seen in normal animals - 62 ± 6 per cent of initial level versus 84 ± 5 per cent - ($p < 0.05$). Denervated animals also showed a brief bradycardia 213 ± 27 to 197 ± 24 beats per minute ($p < 0.02$) lasting for 2 minutes instead of the tachycardia noted in normal animals. The results are listed in Table I and Figure 2.

DISCUSSION

Etomidate in the dosage used (0.8 mg/kg) has been shown to cause a marked and long-lasting depression of sympathetic activity almost unreflected by changes in arterial pressure. Since the mild tachycardia noted in normal animals can only in part have counteracted the depression in arterial pressure expected from the severely depressed sympathetic tone, it appears likely that the direct cardiovascular depressant action of etomidate is minimal. When baroreceptor-denervated animals responded to etomidate with bradycardia instead of tachycardia it might be due in part to the depressed sympathetic tone and in part to a direct negative chronotropic effect of etomidate which deserves further studies.

The slow return of sympathetic tone appears somewhat in contrast to the postulated fast metabolism of the drug,¹ but this might be explained in part on the basis of the dosage of the drug used.

The tachycardia seen in normal animals in spite of depressed sympathetic tone, on the other hand, especially when related to the findings in denervated animals, can only be explained on the basis of a vagolytic action of etomidate.

SUMMARY

We have studied the effects of etomidate on preganglionic cervical sympathetic activity, arterial pressure, and pulse rate.

FIGURE 2. A typical response to etomidate 0.8 mg/kg given to a normal cat. Only a short period of hypotension and tachycardia is noted whereas sympathetic tone is almost abolished and stays depressed for twenty minutes. (Dotted pressure line on arterial pressure indicates units in S.I. scale (kilo-pascal).) Heart rate (Hz) can be derived from beats/min by dividing with a factor of 60.

TABLE I
EFFECTS OF ETOMIDATE ON SYMPATHETIC NERVOUS ACTIVITY, MEAN ARTERIAL BLOOD PRESSURE AND PULSE RATE IN NORMAL AND BARORECEPTOR-DENERVATED CATS. ALL VALUES ARE MEAN OF FIVE EXPERIMENTS (ANIMALS). STATISTICAL SIGNIFICANT CHANGES FORM INITIAL VALUES ARE EXPRESSED BY A P-VALUE

Sympathetic activity (imps/sec)		Initial value	High	Low	Percent of initial	1	2	3	4 minutes	5	10	20	30
Normal cats	Mean	48		4	9	12	15	17	16	15	22	34	37
	SE	7		2	6	3	4	5	3	3	6	8	6
	P			0.01		0.02	0.02	0.05	0.02	0.02	0.05		
Denervated cats	Mean	59		5	9	11	20	20	24	27	27	44	49
	SE	8		2	4	3	4	3	4	4	9	8	8
	P			0.01		0.01	0.01	0.002	0.05	0.05	0.05		
Mean arterial pressure													
Normal cats	Mean	128		108	84	119	130	129	129	130	116	126	123
	SE	7		8	5	7	7	6	5	5	8	5	3
	P			0.05									
Denervated cats	Mean	127		67	62	81	95	108	123	132	133	122	126
	SE	16		17	6	8	18	16	19	19	20	16	17
	P			0.01		0.01	0.05	0.05					
Pulse rate beats/min													
Normal cats	Mean	182	214			211	201	192	189	185	163	167	166
	SE	11	14			15	15	13	14	13	6	9	6
	P		0.05			0.05							
Denervated cats	Mean	213		197		198	204	207	209	210	211	209	210
	SE	27		24		24	25	27	28	27	27	27	26
	P			0.02		0.05							

Normal and baroreceptor-denervated animals were studied. On the basis of findings it is concluded that etomidate exerts a minimal direct depressant action on the cardiovascular system. A profound depression of sympathetic tone was observed in spite of unaffected arterial pressure. Etomidate was also shown to possess a mild vagolytic action.

RÉSUMÉ

Nous avons étudié les effets de l'etomidate sur l'activité sympathique pré-ganglionnaire cervicale, sur la pression artérielle et sur la fréquence cardiaque du chat. Cinq animaux normaux et cinq autres animaux en état de dénervation baso-réceptrice ont été étudiés.

Nos résultats indiquent que l'etomidate exerce une action dépressive directe minime sur le système cardiovasculaire. On a cependant observé une dépression profonde du système sympathique même si la tension artérielle n'était pas modifiée. Nous avons également mis en évidence une action vagolytique légère de l'etomidate.

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