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Effect of Etomidate on the Cardiovascular System

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Following intravenous injection of 0.3 mg/kg of etomidate, the only noteworthy change in measured cardiovascular parameters was a 10 percent increase in heart rate. This suggests relatively stable cardiovascular response associated with administration of this new nonbarbiturate anesthesia induction agent.

ETOMIDATE is a new ultrashort-acting nonbarbiturate agent advocated for induction of general anesthesia.[1,2] One of the featured characteristics of etomidate is its short duration of action. According to animal preparations, hydrolysis appears to occur mainly in the liver, and to a lesser degree in the blood, with metabolites peaking within 7 minutes following IV administration.[3,4] Release of histamine does not occur with etomidate.[5] Apnea, if it occurs, is only transient, with spontaneous ventilation returning within approximately 90 seconds.[1,4] Preliminary reports have suggested cardiovascular stability following IV administration in dogs and humans.[6-8] In order to confirm previous reports, we elected to study the cardiovascular effects of etomidate in human volunteers.

MATERIALS AND METHODS

Eleven patients, 4 men and 7 women, ASA class I-III, ranging in age from 24 to 65 years (mean 43.09) were studied after informed consent was obtained from each. All patients received diazepam (10 mg) and atropine (0.4 mg) as premedication. Prior to induction, an 18-gauge catheter was inserted percutaneously into a radial artery. Also, a 7-French, quadruple lumen, thermistor-tip, balloon flotation catheter* was introduced via the internal jugular vein into the pulmonary artery. In order to avoid the influence of pain from use of a peripheral vein, etomidate was injected through the central venous lumen of the pulmonary artery catheter (at a dose of 0.3 mg/kg, administered over a period of 30 to 60 seconds).

With subjects supine, measurements of mean systemic arterial pressure (MSAP), mean pulmonary artery pressure (MPAP), central venous pressure (CVP), and pulmonary-capillary wedge pressure (PCWP) were made at end-expiration†. Measurements were recorded over 3 respiratory cycles, 3 minutes before induction and between 2 and 4 minutes after induction‡. Cardiac output (CO) was determined in duplicate, employing the thermodilution method§. Values of CO were accepted within ± 0.5 L/min (mean difference = 0.075 L/min); if results deviated from these limits, a 3rd determination was obtained. Patients were not stimulated, and O_2 was administered throughout the study period. From

*Edwards Laboratories #93A-118-7F.
†American Optical #5145 pressure transducers.
‡American Optical portable pressure recorder.
§Edward's Laboratory #9510 computer.

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TABLE
Effect of Etomidate on Cardiovascular Parameters

	n	χ pre-etomidate	χ post-etomidate	SD	Percent change	Prob $>t$
HR	11	92.64	101.55	13.85	10.0	0.0586*
MSAP	11	94.10	91.21	8.20	3.0	0.2713
MPAP	11	15.91	15.97	4.43	0.4	0.9645
PCWP	11	9.18	9.64	3.59	5.0	0.6832
CVP	4	5.00	5.00	2.58	0.0	1.0000
SV	11	61.36	58.35	13.92	5.0	0.5117
CI	11	2.92	2.91	0.27	0.2	0.9546
SVR	11	1830.22	1785.92	77.97	2.0	0.3384
PVR	11	109.62	89.83	72.78	18.0	0.4122

*Significance borderline.

MSAP, MPAP, CVP, PCWP, body surface area (BSA), and heart rate (HR), the following parameters were derived (according to formulas in the Appendix): Stroke volume (SV), cardiac index (CI), systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR). Data were analyzed by paired Student's *t*-test (values of $p<0.05$ being of statistical significance) with the aid of a Hewlett-Packard computer-calculator*. Due to technical difficulties, CVP was recorded in only 4 patients.

RESULTS

Of all measured parameters (table), the 10 percent increase in HR ($p = 0.0586$, significance borderline) was the only notable change. The decrease of 18 percent in pulmonary vascular resistance was not of statistical significance, due to the large value of standard deviation.

DISCUSSION

A slight increase (10%) in heart rate was the only hemodynamic change noted to be of significance. Since completion of our study, we have become aware of the similar work of Rifat's group.[9] Their results following the injection of 0.2 mg/kg of etomidate in 14 patients strikingly resemble ours, with the difference that they noted only a 2.8 percent increase in HR, while PCWP measurements were not recorded. Kettler and coworkers[6] noted a 9 percent increase in HR following 0.3 mg/kg etomidate in 5 cardiac surgery patients.

To be sure, the scope of cardiovascular surgery is expanding and the requirements for ideal anesthetizing agents will expand as well. The need for an induction agent which lacks adverse cardiovascular side effects is well appreciated.

A disadvantage associated with the use of etomidate is pain on injection.[1,2,10] Pain is most prominent when the drug is injected into a peripheral vein. Another drawback is the occurrence of myoclonia.[1,2] The pH of etomidate solution was extremely acidic (pH = 3.4). It is hoped that changing the vehicle of the solution from water to propylene glycol will raise the pH to 5.5 and thereby alleviate pain on injection. Future studies are planned to evaluate whether the incidence and degree of myoclonia may effectively be reduced by the use of proper premedication[1,10] and to determine the effect of a higher pH on the incidence of venous pain.

To the previously reported advantages associated with the use of etomidate, including short duration of action, freedom of histamine release, and minimal respiratory depression, may be added absence of cardiovascular changes. On the basis of these advantages, we feel further investigation with etomidate as an anesthetic induction agent is warranted.

APPENDIX

SV (ml/beat) = (CO/HR) $\times 10^3$

CI (L/min/m^2) = CO/BSA

SVR (dyne sec cm^{-5}) = (MSAP/CO) $\times$ 80

PVR (dyne sec cm^{-5}) = (MPAP − PCWP)/CO $\times$ 80

*Model #9815A.

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SODIUM NITROPRUSSIDE AS CORONARY VASODILATOR. The effect of the intra-arterial injection of 5 to 10 μg of sodium nitroprusside (SNP) on the caliber of normal and diseased coronary arteries was evaluated in 21 patients during diagnostic cardiac catheterization. In addition, the effect of intragraft injection of 5 μg of the same agent on the blood flow in aorta-right coronary artery saphenous vein bypass grafts was also evaluated intraoperatively in 2 patients. SNP induced an increase in the caliber of both normal and stenosed coronary arteries as well as an increase of flow in the grafts. Consistent with measurements of coronary flow response to SNP, angina pectoris, which developed in 4 patients during cardiac catheterization, was immediately relieved and the ischemic ST-segment depression significantly reversed after injection of 5 to 10 μg of the drug into the left main coronary artery. Within the dose range used, SNP caused no significant effect on systemic blood pressure or apparently deleterious electrophysiologic changes. No side effects were observed. The primary direct action of SNP on the human coronary artery is vasodilatory. *(Yeh BK, Gosselin AJ, Swaye PS, et al: Sodium nitroprusside as coronary vasodilator in man. 1. Effect of intracoronary sodium nitroprusside on coronary arteries, angina pectoris and coronary blood flow. Am Heart J 93:610-616, 1977)*