CARDIOVASCULAR EFFECTS OF ETOMIDATE WITH EMPHASIS ON REGIONAL MYOCARDIAL BLOOD FLOW AND PERFORMANCE

O. PRAKASH, K. M. DHASMANA, P. D. VERDOUW AND P. R. SAXENA

SUMMARY

The effects of 30-min infusions of etomidate 0.03, 0.06, 0.12 and 0.24mg kg\(^{-1}\) min\(^{-1}\) on systemic and regional haemodynamic variables and cardiac performance and metabolism were studied in pigs. The drug caused moderate, but dose-dependent, decreases in the cardiac output, arterial pressure and \(LVdP/dr_{max}\). Myocardial wall thickening, measured by echographic analysis, was decreased by the drug. However, heart rate, myocardial blood flow distribution and myocardial metabolism of lactate, glucose and free fatty acids remained unchanged. Cerebral blood flow was decreased substantially. However, renal blood flow changed only slightly.

ANAESTHETIC AGENTS ADMINISTERED I.V. TO INDUCE ANAESTHESIA MAY DEPRESS THE CIRCULATORY SYSTEM (van Ackern, Deuster and Mast, 1972; Beer and Soga, 1971; Doenicke et al., 1974). Moreover, the doses required for a rapid onset of anaesthesia may produce undesirable side effects and are a possible cause of mortality (Goldstein and Keats, 1970). Etomidate, a new, short-acting non-barbiturate hypnotic agent, has been introduced as a potent anaesthetic agent with a wide safety margin in comparison with conventional drugs (Janssen, Niemegeers and Marsboom, 1975). Both basic and clinical studies have indicated that etomidate produced minimal cardiovascular depression (Weymar et al., 1974; Skovsted and Sapthavichaikul, 1977; Hughes and MacKenzie, 1978; Colvin et al., 1979; Gooding et al., 1979). However, more detailed cardiovascular studies, demonstrating the effect of etomidate on regional myocardial blood flow, performance and metabolism, are lacking. The present study was designed to document these effects in domestic swine.

METHODS

General preparation

Yorkshire pigs (20–30 kg) were prepared as described previously (Verdouw, Deckers and O. PRAKASH,* M.D. (Department of Cardiac Anaesthesia), K. M. DHASMANA, M.D., P. D. VERDOUW (Department of Experimental Cardiovascular Research), P. R. SAXENA, M.D. (Department of Pharmacology). Faculty of Medicine, Erasmus University, Rotterdam, The Netherlands.

*Address for correspondence: Anaesthesiology, Thorax Centre, Academisch Ziekenhuis Rotterdam Dijkzigt, Dr Molewaterplein 40, 3015 GD Rotterdam, The Netherlands.

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through the atrial appendage for the injection of radioactive microspheres.

Regional blood flow measurements

The pattern of blood flow distribution in the heart, lungs, kidneys and the brain was determined by using the radioactive microsphere technique which provides a reasonably accurate and reproducible assessment of regional blood flow in animals (Rivas et al., 1976; Heymann et al., 1977; Johnston and Saxena, 1978; Saxena et al., 1978; Schamhardt et al., 1979; Verdouw, Saxena et al., 1980). About 3–5 × 10⁶ microspheres (15 μm diameter; 3M Co.), labelled with gamma-emitting nuclide iodine-125, cerium-141, strontium-85 or niobium-95 and suspended in saline 1 ml containing a drop of Tween 80, were deaggregated in an ultrasonic bath and injected into the left atrium. The atrial catheter was subsequently flushed with saline. Starting 5 s before the injection of microspheres, a reference arterial blood sample was withdrawn from the aorta (rate 7.8 ml min⁻¹) over a period of 60–65 s. At the conclusion of the experiment, the animal was bled to death and the heart, lungs, kidneys and brain were removed. The last three organs were washed with water, weighed, immediately cut into small pieces, and placed in scintillation counter vials. The heart was kept in 1% formalin for 24 h and handled as described previously (Schamhardt et al., 1979). Briefly, the left ventricle was sectioned into four transverse rings of approximately equal size and thickness, and sections representing the base and apex of the left ventricle were divided into anterior, medial, posterior and lateral regions. Regions at the apex were divided into epicardial and endocardial layers. The other three parts were divided into four equal transmural layers designated from endocardium to epicardium as endo-1, endo-2, epi-1 and epi-2.

Each vial containing the tissues and blood samples was counted for radioactivity in a Nuclear Chicago scintillation counter with preset windows discriminating the different isotopes. The data were analysed by a PDP 11 computer (Saxena et al., 1981) using the spectral stripping technique (Hales, 1974; Heymann et al., 1977). Blood flow (Q) to different tissues was calculated from the equation:

\[ Q_\text{r} = Q_\text{t} \left( \frac{C_\text{r}}{C_\text{t}} \right) \]

where

\[ Q_\text{r} = \text{rate of withdrawal of the reference blood sample} \]

\[ C_\text{r} = \text{radioactivity counts in reference samples of blood} \]

\[ C_\text{t} = \text{radioactivity counts in tissue} \]

The percentage of cardiac output delivered to the tissues was calculated by multiplying the ratio of tissue blood flow and cardiac output by 100.

Regional myocardial wall thickness measurements

Tracings of myocardial wall thickness were obtained with a 5-MHz ultrasonic transducer (Krautkramer-Branson, U.S.A.) sutured onto a part of the epicardial surface perfused by LAD. The echocardiogram, the pressures in the left ventricle and in the root of the aorta and the rate of change of ventricular pressure (LV dP/dt) were recorded continuously on linagraph direct-print photographic paper using a Honeywell fiberoptic system (Verdouw, ten Cate et al., 1980). The tracings were analysed on a digitizing tablet connected to a PDP-11/10 computer (van Zwieten et al., 1979) to derive the end-diastolic wall thickness (EDT; end-diastole was defined as the occurrence of the upstroke of LV dP/dt), the end-systolic wall thickness (EST; end-systole was defined as the occurrence of the incisura of the central aortic pressure tracing), systolic time interval (STI), systolic wall thickening (SWT = [(EST – EDT)/EDT] × 100%), and the mean velocity of systolic wall thickening (\( V_{\text{SWT}} \)). The latter was calculated as the ratio of SWT and the duration of systole (that is the isovolumic contraction phase and the left ventricular ejection time). Each value was determined as the average of five consecutive beats, all analysed in duplicate.

Biochemical analysis

Arterial and coronary venous blood samples were analysed for glucose, free fatty acid (FFA) and lactate concentrations. Plasma was separated and frozen for subsequent determination of glucose (on an autoanalyser using Technicon methodology) and FFA (Trout, Estes and Friedberg, 1960). Whole blood was immediately deproteinized with an equal volume of cold 8% perchloric acid and the supernatant was frozen for lactate determination (Apstein, Puchner and Brachfeld, 1970) at a later date. The arterial blood etomidate concentration was determined by gas chromatography using the method described by de Boer, Smeekens and Breimer (1979).
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Experimental programme
Base-line values were obtained after the animal had been in a steady haemodynamic state for at least 30 min following the completion of surgery. Subsequently, four doses of etomidate (0.03, 0.06, 0.12 and 0.24 mg kg\(^{-1}\) min\(^{-1}\)), dissolved in 0.9% sodium chloride were infused at intervals of 30 min at a rate of 30 ml h\(^{-1}\). The haemodynamic variables were obtained at intervals of 5, 10 and 20 min while the blood samples were withdrawn with the last set of recordings. The microspheres, labelled with different isotopes, were injected at the base-line and 20 min after the first three doses of the drug.

Statistical analyses
The data are presented as mean ± SEM. Since there was no appreciable difference between the data obtained after 5, 10 or 20 min following the start of the etomidate infusion, only the last set of data has been presented. The effect of etomidate, unless otherwise stated, is shown as percent change from the respective base-line values. Student’s paired t test was used to evaluate the statistical significance of the drug-induced changes in the haemodynamic and biochemical variables. Correlations between two variables were calculated by the use of Spearman rank test. A P-value of less than 0.05 (one-tail) was considered to be statistically significant.

RESULTS
Etomidate blood concentration
After four different doses of etomidate (0.03, 0.06, 0.12 and 0.24 mg kg\(^{-1}\) min\(^{-1}\)), the concentration of the drug in the blood 20 min after the start of the infusion was found to be 0.44 ± 0.03 (n = 6), 1.10 ± 0.04 (n = 5), 2.65 ± 0.38 (n = 6) and 7.59 ± 0.79 (n = 7) µg ml\(^{-1}\), respectively.

Systemic haemodynamic variables
Table I depicts the haemodynamic values before and after the administration of etomidate. Etomidate produced a dose-dependent decrease in aortic pressure, cardiac output and LV dP/dt max. Since heart rate did not change significantly, the decrease in stroke volume appeared to be mainly responsible for the decrease in the cardiac output. Peripheral resistance did not change significantly.

Regional haemodynamic variables
Precision of microsphere technique. The precision of the microsphere technique, as used by us in the pigs, is indicated by comparing the values of blood flow to related organs. For example, the blood flows to left and right kidneys, when measured simultaneously (n = 23 in six pigs), were 3.48 ± 0.14 and 3.48 ± 0.13 ml min\(^{-1}\), respectively, and they showed excellent correlation \(R_s = 0.9496; P < 0.001\). Similarly, simultaneous measurements (n = 19) of the blood flows in the left anterior descending coronary artery (LAD) using the electromagnetic flowmeter (43.8 ± 4.0 ml min\(^{-1}\)) and in the corresponding segment of the myocardium (33.5 ± 3.2 ml min\(^{-1}\)), although differing in absolute terms, also correlated significantly \(R_s = 0.6371; P < 0.001\). The difference in the absolute, values must apparently be the result of (a) an inherent error in the precise localization of the LAD-perfused area and (b) animal-to-animal variability in the calibration factor of the flow probe. This contention is supported by the fact that the changes, occurring after the administration of the

<table>
<thead>
<tr>
<th>Variables</th>
<th>Base-line values</th>
<th>0.03</th>
<th>0.06</th>
<th>0.12</th>
<th>0.24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (min(^{-1}))</td>
<td>128 ± 6</td>
<td>4 ± 5</td>
<td>-8 ± 7</td>
<td>-9 ± 10</td>
<td>-18 ± 9</td>
</tr>
<tr>
<td>Systolic arterial pressure (mm Hg)</td>
<td>106 ± 5</td>
<td>-7 ± 3*</td>
<td>-10 ± 4*</td>
<td>-16 ± 5*</td>
<td>-26 ± 7*</td>
</tr>
<tr>
<td>Diastolic arterial pressure (mm Hg)</td>
<td>63 ± 5</td>
<td>-10 ± 4*</td>
<td>-12 ± 4*</td>
<td>-20 ± 7*</td>
<td>-33 ± 7*</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>88 ± 5</td>
<td>-10 ± 2*</td>
<td>-14 ± 3*</td>
<td>-20 ± 5*</td>
<td>-30 ± 5*</td>
</tr>
<tr>
<td>Cardiac output (litré min(^{-1}))</td>
<td>4.18 ± 0.40</td>
<td>-11 ± 2*</td>
<td>-19 ± 4*</td>
<td>-28 ± 4*</td>
<td>-41 ± 3*</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>33 ± 3</td>
<td>-13 ± 6*</td>
<td>-9 ± 9*</td>
<td>-17 ± 8*</td>
<td>-22 ± 9*</td>
</tr>
<tr>
<td>LVdP/dt max (mm Hg s(^{-1}))</td>
<td>3700 ± 431</td>
<td>-11 ± 6</td>
<td>-29 ± 10*</td>
<td>-41 ± 11*</td>
<td>-64 ± 5*</td>
</tr>
<tr>
<td>Total peripheral resistance (mm Hg litre(^{-1}) min)</td>
<td>21 ± 2</td>
<td>3 ± 5</td>
<td>8 ± 8</td>
<td>13 ± 13</td>
<td>20 ± 13</td>
</tr>
</tbody>
</table>
Table II. Effect of etomidate on regional distribution of cardiac output and blood flow in six pigs. Values are mean ± SEM. †Values represent blood flow (litre min⁻¹). ‡Nutrient part of cardiac output was calculated by subtracting the AVA fraction from cardiac output. *Significant (P<0.05) change from the base-line value.

<table>
<thead>
<tr>
<th>Organ/tissue</th>
<th>Base-line values</th>
<th>% Cardiac output</th>
<th>% Change with etomidate (mg kg⁻¹ min⁻¹)</th>
<th>Blood flow (ml min⁻¹ per 100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.03</td>
<td>0.06</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>(mg kg⁻¹ min⁻¹)</td>
<td></td>
</tr>
<tr>
<td>Lungs (AVA-flow)</td>
<td>20 ± 3</td>
<td>8 ± 18</td>
<td>9 ± 26</td>
<td>39 ± 44</td>
</tr>
<tr>
<td>Nutrient COJ</td>
<td>80 ± 3</td>
<td>-3 ± 5</td>
<td>1 ± 7</td>
<td>-3 ± 9</td>
</tr>
<tr>
<td>Left kidney</td>
<td>5.9 ± 0.4</td>
<td>1 ± 4</td>
<td>10 ± 14</td>
<td>20 ± 12</td>
</tr>
<tr>
<td>Right kidney</td>
<td>6.0 ± 0.5</td>
<td>1 ± 4</td>
<td>11 ± 14</td>
<td>20 ± 11</td>
</tr>
<tr>
<td>Kidneys</td>
<td>12.0 ± 0.9</td>
<td>1 ± 4</td>
<td>10 ± 14</td>
<td>20 ± 12</td>
</tr>
<tr>
<td>Brain</td>
<td>1.2 ± 0.1</td>
<td>29 ± 4*</td>
<td>33 ± 7*</td>
<td>36 ± 9*</td>
</tr>
</tbody>
</table>

Table III. Effect of etomidate on regional myocardial perfusion in six pigs. Values are mean ± SEM. †Calculated as ((arterial O₂ saturation - coronary venous O₂ saturation)/arterial O₂ saturation) × 100%; ‡Calculated as (arterial O₂ saturation - coronary venous O₂ saturation) × coronary blood flow (ml min⁻¹); §Calculated as double product of heart rate (min⁻¹) × left ventricular systolic pressure (cm Hg); ¶Ratio of endocardium 1 and epicardium 2 blood flow.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Base-line values</th>
<th>% Change by etomidate (mg kg⁻¹ min⁻¹)</th>
<th>0.03</th>
<th>0.06</th>
<th>0.12</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAD blood flow (ml min⁻¹)</td>
<td>51 ± 11</td>
<td>-5 ± 17</td>
<td>-21 ± 17</td>
<td>-17 ± 16</td>
<td></td>
</tr>
<tr>
<td>Myocardial O₂ extraction</td>
<td>60 ± 2</td>
<td>1 ± 2</td>
<td>2 ± 3</td>
<td>1 ± 5</td>
<td></td>
</tr>
<tr>
<td>Myocardial O₂ uptake</td>
<td>2637 ± 659</td>
<td>-2 ± 20</td>
<td>-16 ± 20</td>
<td>-20 ± 17</td>
<td></td>
</tr>
<tr>
<td>Myocardial O₂ demand</td>
<td>1388 ± 143</td>
<td>-1 ± 9</td>
<td>-16 ± 11</td>
<td>-24 ± 11</td>
<td></td>
</tr>
</tbody>
</table>

Blood flow to lungs, kidneys and the brain. The base-line measurements of blood flow to lungs, kidneys and the brain, together with percent changes after infusion of etomidate, are shown in table II. Blood flow to lungs, as measured with 15-μm microspheres, represents almost entirely the arteriovenous anastomotic (AVA)-flow (Johnston and Saxena, 1978; Saxena et al., 1978; Schamhardt et al., 1979). In the present series of experiments, the lungs received 20% of cardiac output (equivalent to 0.78 litre min⁻¹ of blood flow). In spite of a decrease in cardiac output, the total blood flow to the lungs (AVAs) remained unaltered because of a moderate, but statistically insignificant, increase in the fraction of cardiac output delivered to the lungs. Hence, the decrease in cardiac output was mainly at the expense of the nutrient (capillary) fraction which decreased following infusion of etomidate (table II).

The left and right kidneys received nearly identical flows (390 and 387 ml min⁻¹ per 100 g, respectively) at base-line. Although etomidate moderately decreased renal blood flow, the changes were significant only after the first dose. Etomidate decreased cerebral blood flow by 35–50% of its base-line value. The changes in the three subdivisions of the brain (forebrain, cerebellum and brain stem) were similar.

three concentrations of etomidate, in the base-line flow values measured by the two techniques exhibited a better correlation (Rₛ = 0.9041; n = 14; P<0.001).
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Regional myocardial blood flow. Table III presents the results of etomidate on coronary blood flow, indices of myocardial oxygen balance and on the distribution of transmural blood flow within the left ventricular myocardium. The drug had only minor effects on myocardial blood flow and oxygen demand and the total myocardial oxygen extraction and uptake showed minimal changes. The transmural distribution within the left ventricular myocardium was not modified by the drug and, consequently, the endo-epi blood flow ratio remained unaltered.

Regional myocardial wall thickness
The base-line values of myocardial wall thickness variables in the six pigs were: systolic time interval (STI), 270 ± 17 ms; end-diastolic wall thickness (EDT), 10.2 ± 0.5 mm; end-systolic wall thickness (EST), 15.5 ± 0.9 mm; systolic wall thickening (SWT), 52 ± 5% and mean velocity of systolic wall thickening (\( V_{SWT} \)), 1.91 ± 0.17 s⁻¹. The values of these variables are similar to those reported previously (Schamhardt et al., 1979; Verdouw, ten Cate et al., 1980; Verdouw, Saxena et al., 1980). We have demonstrated previously that the wall thickness variables remain constant for periods of over 2 h.

The administration of etomidate decreased significantly and in a dose-dependent manner EST, SWT and \( V_{SWT} \) without affecting EDT (fig. 1). The changes induced by the drug in EST and SWT were less than that in \( V_{SWT} \) because STI increased in a dose-dependent manner. Diastolic bulging, which is an indication of myocardial underperfusion (Schamhardt et al., 1979; Verdouw, ten Cate et al., 1980) did not appear after etomidate.

Biochemical variables
Although etomidate did not significantly alter lactate uptake or extraction by the heart tissue, there was a significant increase in arterial lactate concentration after each dose of etomidate. The base-line value of 4.5 ± 0.8 mmol litre⁻¹ increased to 5.8 ± 1.2 mmol litre⁻¹ (\( P < 0.05, n = 7 \)) at the greatest dose. On the other hand, etomidate significantly decreased the initial arterial glucose concentration (5.6 ± 0.4 mmol litre⁻¹) at the three greatest doses (3.9 ± 0.6 mmol litre⁻¹ (\( P < 0.05, n = 6 \)) at 0.24 mg kg⁻¹ min⁻¹ etomidate) without affecting its uptake or extraction. The arterial FFA concentration decreased significantly at the greatest dose from 550 ± 86 μmol litre⁻¹ to 363 ± 98 μmol litre⁻¹ (\( P < 0.05, n = 7 \)), while the myocardial FFA uptake decreased significantly (\( P < 0.05 \)) at the two greatest doses from the base-line value of 6.3 ± 1.3 μmol min⁻¹ to 2.0 ± 1.3 and 1.5 ± 0.8 μmol min⁻¹, respectively. There were no significant changes in FFA extraction.

DISCUSSION

Animal preparation
Baseline measurements of the pharmacological effects of anaesthetic agents can be obtained either from unanaesthetized, pre-instrumented animals or from animals under light basal anaesthesia. Although the use of awake animals might be preferred, elaborate measurements in unanaesthetized pigs of the cardiovascular and biochemical variables, such as those performed in the present investigation, would present formidable
problems and, with it, show considerable variability. For this reason, we decided to study the effects of etomidate under the background of basal anaesthesia attained with a mixture of nitrous oxide and oxygen, together with a continuous infusion of a neuroleptic agent, azaperone, and a neuromuscular blocker, pancuronium. Initially, about 90 min before the start of the experiment, metomidate had been given to decrease the effects of surgical trauma. Our previous investigations (Verdouw et al., 1978; Verdouw, Deckers and Conard, 1979; Verdouw et al., 1979) have shown that the cardiovascular variables remain relatively stable under this anaesthetic regimen.

**Etomidate infusion**

To avoid the influence of rapid bolus injections on the cardiovascular and biochemical variables, etomidate was administered by an i.v. infusion. The smallest dose (0.03 mg kg\(^{-1}\) min\(^{-1}\)) is the one which, after an initial loading dose of about 0.25 mg kg\(^{-1}\), provides adequate surgical anaesthesia in patients (van Dijk, 1979; de Ruijter et al., 1979). The plasma concentrations (0.44 ± 0.03 μg ml\(^{-1}\)) measured 20 min after etomidate 0.03 mg kg\(^{-1}\) min\(^{-1}\) agreed well with those reported in patients (van Dijk, 1979; de Ruijter et al., 1979). Infusion of greater doses (0.06, 0.12 and 0.24 mg kg\(^{-1}\) min\(^{-1}\)) resulted in a marked increase in the plasma concentration of the drug. Since the plasma half-life of etomidate is more than 200 min (van Hamme, Ghonein and Ambre, 1978; de Ruijter et al., 1979), the drug concentration may not have reached a steady state. Yet, a disproportionately greater increase of the plasma concentration after the highest dose (0.24 mg kg\(^{-1}\) min\(^{-1}\)) in comparison with the lower doses, indicated partial saturation of the esterases which hydrolyse etomidate (Heykants et al., 1975).

**Systemic and regional haemodynamics**

Earlier investigations revealed that etomidate, in comparison to other i.v. anaesthetic agents, produced less cardiovascular depression (Doenicke et al., 1973; Doenicke et al., 1974; Holdcroft et al., 1976; Patschke et al., 1977b; Colvin et al., 1979). We observed that etomidate decreased the systemic arterial pressure, stroke volume, cardiac output, \(LVdP/dt\max\) and myocardial wall thickness in a dose-dependent manner; changes which were relatively minor following the lowest dose—a dose approximately equivalent to that required for surgical anaesthesia.

The decrease in the cardiac output, particularly with the high doses, appeared to result from a number of factors: (1) a decrease in sympathetic outflow from the central nervous system (Skovsted and Sapthavichaikul, 1977; Hughes and MacKenzie, 1978), (2) vascular autoregulation as a result of a decrease in the metabolic needs of the tissues as indicated by selective decrease in the nutrient part of the cardiac output and (3) a decrease in the stroke volume resulting from reduced filling pressure. It does not seem likely that etomidate has an important direct depressant effect on the myocardium since such an effect, obtained after bolus injections of large doses (2–8 mg kg\(^{-1}\)), lasts for only a few minutes (Hughes and MacKenzie, 1978). Moreover, the blood concentrations needed to depress the myocardial contractility in cat heart–lung preparation exceeded 15 μg ml\(^{-1}\) (Fischer and Marquortt, 1977); such high drug concentrations were not achieved even after the highest dose of etomidate in our experiments. Therefore, the reduction of \(LVdP/dt\max\), \(\Psi\), and SWT following etomidate could be secondary to changes in the pre- and after-load of the heart.

Evaluation of regional blood flow with the radioactive microsphere technique revealed that etomidate decreased renal and cerebral blood flows. While the potential decrease of renal blood flow was counteracted by a moderate increase in the fraction of cardiac output delivered to the kidneys, both the distribution of cardiac output and blood flow to the brain were markedly decreased by etomidate in a dose-dependent manner. As already demonstrated in man, the decrease in the cerebral blood flow is secondary to a decrease in brain metabolism (Herrschaft et al., 1975; Renou et al., 1978). Although there was a tendency for myocardial oxygen demand, oxygen uptake and blood flow to decrease, the changes were not significant with any of the doses studied. Clinical investigations have also shown that etomidate has only a slight effect on myocardial oxygen balance (Kettler et al., 1974; Patschke et al., 1977a). Furthermore, there was no transmural redistribution of myocardial blood flow.

**Biochemical variables**

It is known that a combination of azaperone–etomidate anaesthesia yields rather high
arterial lactate concentrations (Verdouw et al., 1979). In the present experimental set-up we observed a high baseline arterial concentration of lactate, and etomidate further increased arterial lactate values at all doses. Since the blood-gas tensions did not change, it appears that etomidate, like phenformin (Williams and Port, 1974), may inhibit cellular respiration to increase arterial lactate concentration. In addition, etomidate decreased arterial glucose concentrations, which may have been converted to lactate. In the greatest dose, FFA concentrations decreased, probably as a result of inhibition of lipolysis. Myocardial uptake and extraction of lactate and glucose remained unaltered after the administration of etomidate while myocardial FFA uptake was decreased only by high doses of the drug indicating a decreased supply of FFA to the heart.

In conclusion, the present study shows that etomidate, especially when infused in amounts equivalent to those for inducing surgical anaesthesia, produces minimal changes in the cardiovascular system, particularly regional myocardial blood flow, performance and metabolism.

ACKNOWLEDGEMENTS

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REFERENCES


**EFFETS CARDIOVASCULAIRES ET PERFORMANCES DE L'ETOMIDATE SURTOUT SUR LE DEBIT SANGUIN REGIONAL DU MYOCARDE**

Résumé

Les effets des perfusions d'étomidate d'une durée de 30 min (à raison de 0,03, 0,06, 0,12 et 0,24 mg kg⁻¹ min⁻¹) sur les éléments variables des systèmes hémodynamiques systémiques et régionaux, sur les performances cardiaques et sur le métabolisme ont été étudiés sur des porcs. Ce médicament a provoqué des diminutions modérées, tout en étant fonction de la dose, du débit cardiaque, de la pression arterielle et de la LVdP/dr maxime. L'épaisseur de la paroi du myocarde, mesurée par une analyse échographique, a été réduite par le médicament. Toutefois, la fréquence cardiaque, la répartition du débit sanguin du myocarde, et le métabolisme du lactate, de la glucose et des acides non gras du myocarde sont demeurés sans changement. Le débit sanguin cérébral a sensiblement diminué, mais le débit sanguin rénal n'a été que légèrement modifié.

**HERZKREISLAUF-WIRKUNGEN VON ETOMIDAT MIT BETONUNG VON REGIONALEM MYOKARD-BLUTFLUSS UND LEISTUNG**

Zusammenfassung

Die Wirkungen einer 30 min-Infusion von Etomidat 0,03, 0,06, 0,12 und 0,24 mg kg⁻¹ min⁻¹ auf systemische und regionale variable hämodynamische Werte, Herzleistung und Metabolismus wurden bei Schweinen studiert. Sie bestanden aus mässigen, aber dosisabhängigen Senkungen des Herzminutenvolumens, des arteriellen Drucks und von LVdP/dr max. Verdickung der Myokardwand, gemessen durch echographische Analyse, wurde durch die Droge herabgesetzt. Herztätigkeit, Myokardblutfussverteilung und der myokardiale Metabolismus von Laktat, Glukose und freien Fettsäuren blieben jedoch unverändert. Der zerebrale Blutfuss wurde stark vermindert, der Nierenblutfuss veränderte sich aber nur geringfügig.
Se estudiaron en cerdos los efectos de infusiones de 30 minutos de duración, de 0,03, 0,06, 0,12 y 0,24 mg kg⁻¹ min⁻¹, sobre las variables hemodinámicas regionales y sistémicas, el funcionamiento cardíaco y el metabolismo. La droga ocasionó una disminución moderada, pero que iba en función de la dosis, de la producción cardíaca, de la presión arterial y de LVdP/dt máxima. El aumento del grosor de las paredes del miocardio, medido mediante análisis ecográfico, disminuyó como consecuencia de la droga. Sin embargo, el ritmo cardíaco, la distribución del flujo sanguíneo del miocardio y el metabolismo miocardial de la lactasa, glucosa y de los ácidos carentes de grasas permanece inalterado. El flujo sanguíneo cerebral disminuyó sustancialmente. No obstante el el flujo de sangre renal cambio sólo ligeramente.