HAEMODYNAMIC STUDIES DURING INDUCTION OF ANAESTHESIA FOR OPEN-HEART SURGERY USING DIAZEPAM AND KETAMINE

A. P. F. JACKSON, P. R. DHADPHALE, M. L. CALLAGHAN AND S. ALSERI

SUMMARY

In 14 patients undergoing open-heart operations the haemodynamic effects of diazepam 0.4 mg kg$^{-1}$ followed by ketamine 2 mg kg$^{-1}$ were studied. In eight patients undergoing coronary bypass surgery, the mean arterial pressure decreased significantly after diazepam from 90.3 ± 7.4 (SEM) to 78.0 ± 5.0 mm Hg ($P<0.05$). However, no changes occurred in six patients undergoing valve replacement. The subsequent administration of ketamine produced no significant changes in mean arterial pressure. No significant change in heart rate occurred in any patient at any time during the period of study. No patient reported unpleasant emergence reactions after operation.

Although ketamine has been advocated as an anaesthetic agent for patients undergoing cardiac surgery (Corssen et al., 1970; Lippman and Cleveland, 1971) its stimulant actions on the cardiovascular system are considered generally to be undesirable for patients with valvular (Arani and Carleton, 1967) and coronary artery disease (Tweed, Minuck and Mymin, 1972).

Pretreatment with diazepam has been shown to prevent the increase in plasma concentration of catecholamines associated with ketamine (Zsigmond et al., 1974; Zsigmond, Yoon and Kothary, 1976). It is reasonable to predict that the inhibition of sympathetic nervous activity by diazepam might be expected to minimize the increases in heart rate and mean arterial pressure also. This would be particularly desirable in patients with heart disease, in whom the ability to increase myocardial oxygen supply is strictly limited.

PATIENTS AND METHODS

Fourteen patients undergoing elective open-heart operations were studied. Six patients had cardiac valvular disease and eight had ischaemic heart disease. Patients in the valvular surgery group were in the age range 29–70 yr. The NYHA grading (New York Heart Association Inc., Criteria Committee, 1973) was class III in all but one patient, who was graded as class IV. Values for left ventricular end diastolic pressure (LVEDP) ranged from 7 to 20 mm Hg. There were three aortic and three mitral valve replacements. In the coronary artery surgery group the ages of the patients ranged from 31 to 68 yr. Two patients were in class II, and three each in classes III and IV. Values for LVEDP were between 8 and 18 mm Hg. Digitalis, diuretics and beta-blocking drugs were all discontinued 48 h before operation. Two patients with mitral valve disease exhibited atrial fibrillation. Premedication was with morphine 5–15 mg i.m. and hyoscine 0.4 mg i.m.

In the operating room intravascular cannulae were inserted percutaneously under local anaesthesia: two 14-gauge i.v. cannulae, one 20-gauge radial artery cannula. A 7F triple-lumen flow directed thermodilution balloon catheter was inserted via the right internal jugular vein using a Desilets–Hoffman percutaneous catheter introducer. E.g., systemic arterial, pulmonary arterial and venous pressures were recorded continuously on a Hewlett-Packard 3010 A 4-channel recording system.

Each patient breathed 100% oxygen for 5 min and baseline haemodynamic measurements were obtained. Cardiac output was measured by the thermodilution technique using an Electronics for Medicine Cardiac Output computer model DT CCO-07. Measurements of cardiac output were made in duplicate, and values greater than 10% of each other were rejected. In addition, heart rate, mean arterial pressure, central venous pressure and pulmonary wedge pressure were measured. Arterial blood $P_{O_2}$, $P_{CO_2}$ and pH were measured using an ABL 1 blood-gas analyser.
Diazepam 0.4 mg kg$^{-1}$ i.v. was injected at a rate of 10 mg min$^{-1}$. Three minutes later a second set of haemodynamic values was obtained. Thereafter ketamine 2 mg kg$^{-1}$ was injected i.v. and 3 min later the haemodynamic measurements were repeated.

Throughout the induction sequence the patients breathed 100% oxygen. When necessary, ventilation was assisted manually. If the arterial systolic pressure decreased to less than 80 mm Hg the patient was placed in the Trendelenburg position and Hartmann's solution was infused i.v. After operation the patients were questioned specifically about awareness during the operation or unpleasant dreams during recovery.

Data from the patients with valvular heart disease and coronary heart disease were considered separately and analysed for statistical significance using Student's $t$ test for paired data. A $P$ value of less than 0.05 was considered significant.

### RESULTS

In the coronary bypass graft group mean arterial pressure (MAP) decreased from $90.3 \pm 7.4$ (SEM) to $78.0 \pm 5.0$ mm Hg after diazepam ($P<0.05$), whereas in the valve replacement group there was no significant change in MAP (tables I and II). In both groups the administration of ketamine produced no significant changes in MAP or heart rate compared with either baseline or post-diazepam values. The Stroke Work Index (SWI) was not changed significantly in the coronary bypass graft group, but decreased from $35.2 \pm 6.1$ to $29.1 \pm 5.3$ g m m$^{-2}$ after diazepam in the group with valvular heart disease ($P<0.05$). However, there was no significant change in SWI after ketamine compared with baseline or post-diazepam values in the valvular group.

$PaCO_2$ increased from $5.43 \pm 0.186$ to $6.47 \pm 0.306$ kPa ($P<0.01$) in patients with valvular heart disease.

#### TABLE I. Haemodynamic changes during induction of anaesthesia with diazepam and ketamine in six patients undergoing open-heart surgery for valvular disease (mean ± SEM)

<table>
<thead>
<tr>
<th></th>
<th>Pre-induction (control)</th>
<th>After diazepam</th>
<th>After ketamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beat min$^{-1}$)</td>
<td>$80 \pm 4.6$</td>
<td>$81.5 \pm 5.0$</td>
<td>$73.8 \pm 3.3$</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>$88.3 \pm 4.3$</td>
<td>$83.3 \pm 5.7$</td>
<td>$82.3 \pm 6.2$</td>
</tr>
<tr>
<td>Rate pressure product (litre min$^{-1}$ m$^{-3}$)</td>
<td>$7088.3 \pm 592.7$</td>
<td>$6773.7 \pm 590.0$</td>
<td>$6081.7 \pm 558.2$</td>
</tr>
<tr>
<td>Cardiac index (litre min$^{-1}$ m$^{-3}$)</td>
<td>$2.4 \pm 0.3$</td>
<td>$2.2 \pm 0.2$</td>
<td>$2.0 \pm 0.2$</td>
</tr>
<tr>
<td>Systemic vascular resistance (dyne s cm$^{-2}$)</td>
<td>$1653 \pm 118$</td>
<td>$1693 \pm 262$</td>
<td>$1744 \pm 132$</td>
</tr>
<tr>
<td>Stroke work index (g m m$^{-2}$)</td>
<td>$35.2 \pm 6.1$</td>
<td>$29.1 \pm 5.3^*$</td>
<td>$29.7 \pm 6.2$</td>
</tr>
<tr>
<td>$PaCO_2$ (kPa)</td>
<td>$5.43 \pm 0.186$</td>
<td>$6.4 \pm 0.4^*$</td>
<td>$6.47 \pm 0.306^{**}$</td>
</tr>
</tbody>
</table>

* $P<0.05$; ** $P<0.01$.

#### TABLE II. Haemodynamic changes during induction of anaesthesia with diazepam and ketamine in eight patients undergoing aorto-coronary bypass surgery (mean ± SEM)

<table>
<thead>
<tr>
<th></th>
<th>Pre-induction (control)</th>
<th>After diazepam</th>
<th>After ketamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beat min$^{-1}$)</td>
<td>$74.4 \pm 5.6$</td>
<td>$73.3 \pm 6.0$</td>
<td>$76.4 \pm 6.7$</td>
</tr>
<tr>
<td>Mean arterial pressure (mm Hg)</td>
<td>$90.3 \pm 7.4$</td>
<td>$78.0 \pm 5.0^*$</td>
<td>$80.6 \pm 5.8$</td>
</tr>
<tr>
<td>Rate pressure product (litre min$^{-1}$ m$^{-3}$)</td>
<td>$6789.0 \pm 956.9$</td>
<td>$5864.8 \pm 806.1$</td>
<td>$6356.3 \pm 951.1$</td>
</tr>
<tr>
<td>Cardiac index (litre min$^{-1}$ m$^{-3}$)</td>
<td>$3.1 \pm 0.3$</td>
<td>$2.7 \pm 0.2$</td>
<td>$2.7 \pm 0.3$</td>
</tr>
<tr>
<td>Systemic vascular resistance (dyne s cm$^{-2}$)</td>
<td>$1276 \pm 214$</td>
<td>$1249 \pm 175$</td>
<td>$1241 \pm 141$</td>
</tr>
<tr>
<td>Stroke work index (g m m$^{-2}$)</td>
<td>$43.5 \pm 4.6$</td>
<td>$33.9 \pm 2.0$</td>
<td>$33.8 \pm 2.4$</td>
</tr>
<tr>
<td>$PaCO_2$ (kPa)</td>
<td>$5.39 \pm 0.106$</td>
<td>$5.91 \pm 0.12^{**}$</td>
<td>$5.8 \pm 0.12$</td>
</tr>
</tbody>
</table>

* $P<0.05$; ** $P<0.01$. 

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and from $5.39 \pm 0.106$ to $5.8 \pm 0.12$ kPa ($P < 0.01$) in the group undergoing coronary bypass surgery. All values of pH ranged between 7.37 and 7.30. No value of $P_{a_o_2}$ was less than 20.0 kPa.

All other measurements showed no significant changes after either diazepam or ketamine. In neither group of patients did the changes in MAP necessitate treatment by drugs. No significant cardiac arrhythmia occurred; S–T segment changes were not observed on lead II during induction. On direct questioning after operation no patient reported awareness or unpleasant dreams or emergence reactions.

**DISCUSSION**

These data are presented as an initial report. As there was no control group of patients receiving ketamine alone, this was not a controlled study, but nevertheless under the conditions of this study, the combination of diazepam and ketamine provided satisfactory induction of anaesthesia. Others (Tweed, Minuck and Mymin, 1972; Kopriva, 1974) have documented the well-known cardiovascular stimulant effects of ketamine alone in patients with cardiac disease. Kopriva noted an increase of 123% in rate pressure product (RPP) after ketamine 1.5 mg kg$^{-1}$ in patients undergoing coronary bypass grafting, whereas a slightly larger dose of ketamine in our patients pre-treated with diazepam produced no increase in RPP. This suggests that diazepam modifies the usual stimulant effects of ketamine on the cardiovascular system.

**APPENDIX**

1. Cardiac index (litre min$^{-1}$ m$^{-2}$)
   \[
   \text{Cardiac index} = \frac{\text{cardiac output} \ (\text{litre min}^{-1})}{\text{body surface area} \ (\text{m}^2)}
   \]

2. Systemic vascular resistance (dyne s cm$^{-5}$)
   \[
   \text{Systemic vascular resistance} = \frac{\text{MAP} - \text{CVP} \ (\text{mm Hg})}{\text{cardiac output} \ (\text{litre min}^{-1})} \times 80
   \]

3. Stroke volume index (ml m$^{-2}$)
   \[
   \text{Stroke volume index} = \frac{\text{stroke volume} \ (\text{ml})}{\text{body surface area} \ (\text{m}^2)}
   \]

4. Stroke work index (g m$^{-2}$)
   \[
   \text{Stroke work index} = \text{Stroke volume index} \ (\text{ml m}^{-2}) \times \text{MAP} - \text{pulmonary capillary wedge pressure} \ (\text{mm Hg}) \times 0.0144.
   \]

5. Rate pressure product
   \[
   \text{Rate pressure product} = \text{MAP} \ (\text{mm Hg}) \times \text{heart rate} \ (\text{beat min}^{-1})
   \]

**ACKNOWLEDGEMENT**

We express our appreciation to Drs H. Sloan, M. Kirsh and D. Behrendt of the Section of Thoracic Surgery, University of Michigan Hospital, for their co-operation during this study.

**REFERENCES**

ZUSAMMENFASSUNG

Bei 14 Patienten mit offenen Herzoperationen wurden die hämodynamischen Wirkungen von 0,4 mg kg⁻¹ Diazepam, gefolgt von 2 mg kg⁻¹, studiert. Bei acht Patienten mit Koronar-Umgehungoperationen sank nach Diazepam der mittlere arterielle Druck von 90,3 ± 7,4 (SEM) auf 78,0 ± 5,0 mm Hg (P < 0,05). Bei sechs Patienten, bei denen Herzklappen ersetzt wurden, kamen keine Veränderungen vor. Die anschließende Verabreichung von Ketamin erbrachte keine wesentlichen Veränderungen des mittleren arteriellen Drucks. Bei keinem der Patienten trat zu irgendeiner Zeit während der Studie eine merkliche Veränderung der Herzaktion auf. Kein Patient erlebte unangenehme Reaktionen irgendwelcher Art nach der Operation.

SUMARIO

En 14 pacientes sometidos a operaciones de corazon abierto, se estudiaron los efectos hemodinámicos de diazepam 0,4 mg kg⁻¹, seguido por ketamina 2 mg kg⁻¹. En ocho pacientes sometidos a cirugía de contorneo coronario, la presión arterial media disminuyó significativamente después de diazepam desde 90,3 ± 7,4 (SEM) a 78,0 ± 5,0 mm Hg (P < 0,05). Sin embargo, no se produjeron cambios en seis pacientes sometidos a reemplazo de valvula. La administración posterior de ketamina no produjo cambios significativos en la presión arterial media. No se produjo cambio significativo alguno en la rapidez del corazón durante el periodo de estudio. Ninguno de los pacientes se quejó de reacciones desagradables después de la operación.