PROPOFOL–FENTANYL ANAESTHESIA FOR CORONARY BYPASS SURGERY IN PATIENTS WITH GOOD LEFT VENTRICULAR FUNCTION


Although the efficacy of propofol—as an induction agent—has been studied in patients with coronary artery disease (Patrick et al., 1985), the haemodynamic effects of a maintenance technique, in which propofol was infused continuously in patients about to undergo elective coronary bypass surgery, have not been reported. This study describes the haemodynamic effects associated with induction of anaesthesia using propofol, and the continuous infusion of propofol (supplemented with fentanyl) during the pre-bypass period.

PATIENTS AND METHODS

The design of the study was approved by the Ethical Committee of the Antwerp University Hospital.

Fifteen patients with good left ventricular function (ejection fraction > 55% and left ventricular end diastolic pressure < 14 mm Hg), scheduled for elective coronary bypass surgery were included in the study. Mean age was 53 ± 9 (SD) yr, average weight 75.6 ± 11.2 kg and mean body surface area was 1.87 ± 0.17 m². All patients had angiographically proven coronary artery disease (two- or three-vessel disease); no patient had significant left main coronary artery stenosis. Thirteen patients were taking beta-adrenoceptor antagonists. Five patients had a history of previous infarction, and four other patients had unstable angina. Individual data are presented in table I.

Premedication consisted of fentanyl 0.002 mg kg⁻¹ plus droperidol 0.01 mg kg⁻¹ and glycopyrrolate 0.03 mg kg⁻¹ given i.m. 1 h before surgery, as well as the normal oral medication appropriate to each patient.

Upon arrival of the patient in the operation theatre the electrocardiogram (leads 1, 11 and V5) was continuously displayed. Two large-bore venous cannulae and a 20-gauge Teflon radial arterial catheter were placed under local anaes-
Table I. Clinical data of the investigated patients. All patients received coronary vasodilator therapy. BSA = body square area; NYHA = New York Heart Association classification; AMI = acute myocardial infarction

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>BSA (m²)</th>
<th>NYHA class</th>
<th>History of AMI</th>
<th>Hypertension</th>
<th>Beta-blocking drug</th>
<th>CA² antagonist</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>61</td>
<td>76</td>
<td>1.77</td>
<td>III</td>
<td>+</td>
<td>-</td>
<td>metoprolol</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>51</td>
<td>60</td>
<td>1.62</td>
<td>IV</td>
<td>-</td>
<td>-</td>
<td>metoprolol</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>50</td>
<td>84</td>
<td>2.00</td>
<td>III</td>
<td>+</td>
<td>-</td>
<td>metoprolol</td>
<td>nifedipine</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>59</td>
<td>64</td>
<td>1.80</td>
<td>II</td>
<td>-</td>
<td>-</td>
<td>propranolol</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>51</td>
<td>75</td>
<td>1.90</td>
<td>IV</td>
<td>-</td>
<td>-</td>
<td>metoprolol</td>
<td>diltiazem</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>50</td>
<td>78</td>
<td>1.90</td>
<td>II</td>
<td>-</td>
<td>-</td>
<td>metoprolol</td>
<td>nifedipine</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>69</td>
<td>68</td>
<td>1.75</td>
<td>IV</td>
<td>-</td>
<td>-</td>
<td>—</td>
<td>verapamil</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>42</td>
<td>75</td>
<td>1.93</td>
<td>IV</td>
<td>-</td>
<td>-</td>
<td>atenolol</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>61</td>
<td>90</td>
<td>2.11</td>
<td>III</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>nifedipine</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>43</td>
<td>60</td>
<td>1.64</td>
<td>III</td>
<td>+</td>
<td>-</td>
<td>atenolol</td>
<td>—</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>58</td>
<td>80</td>
<td>1.92</td>
<td>II</td>
<td>-</td>
<td>+</td>
<td>metoprolol</td>
<td>nifedipine</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>67</td>
<td>87</td>
<td>2.09</td>
<td>II</td>
<td>-</td>
<td>-</td>
<td>metoprolol</td>
<td>nifedipine</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>40</td>
<td>84</td>
<td>2.01</td>
<td>III</td>
<td>-</td>
<td>-</td>
<td>atenolol</td>
<td>—</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>65</td>
<td>58</td>
<td>1.53</td>
<td>III</td>
<td>-</td>
<td>-</td>
<td>metoprolol</td>
<td>nifedipine</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>42</td>
<td>95</td>
<td>2.09</td>
<td>III</td>
<td>+</td>
<td>-</td>
<td>metoprolol</td>
<td>nifedipine</td>
</tr>
</tbody>
</table>

The induction dose of propofol was followed by a continuous infusion of propofol. The infusion rate was adjusted in response to changes in systemic arterial pressure, with a maximum rate of 9 mg kg⁻¹ h⁻¹. Before sternotomy an additional dose of fentanyl 0.025 mg kg⁻¹ was given.

Haemodynamic data were recorded and calculated at the following time intervals: before induction, 3 min after induction, 3 min after intubation, before and 3 min after sternotomy and before aortic cannulation. The study was discontinued at the start of extracorporeal circulation.

The following indices of myocardial ischaemia were evaluated every 5 min during the procedure: ST-depression (> 1 mm) in V5, increase in pulmonary capillary wedge pressure (PCWP) or appearance of prominent PCWP v-waves.

Before cardiopulmonary bypass (CPB) was started, heparin 300 u kg⁻¹ was given i.v.; a subsequent dose of pancuronium 0.1 mg kg⁻¹ was given.

Pump priming consisted of 2000 ml of an isotonic solution and 500 ml of a 20% human albumin solution. CPB was conducted using a Bentley TM-10 disposable bubble oxygenator and Stockert/Cobe roller pumps. During CPB the lungs were not ventilated but were allowed to collapse partially with a static inflation pressure of 3 mm Hg.

Patients were cooled during CPB to a rectal temperature of 25 °C. Non-pulsatile flow was used at 2.4 litre m⁻² min⁻¹ with a mean perfusion...
**TABLE II.** Propofol-fentanyl anaesthesia for coronary bypass surgery: haemodynamic data (mean ± SD).

*Significantly different from T1 (P < 0.05). HR = Heart rate; APSyst = systolic arterial pressure; APDiast = diastolic arterial pressure; SVR = systemic vascular resistance; PPsyst = systolic pulmonary artery pressure; PpDiast = diastolic pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure; CVP = central venous pressure; CI = cardiac index; LVSWI = left ventricular stroke work index.

T1 = before induction; T2 = 3 min after induction; T3 = 3 min after intubation; T4 = before sternotomy; T5 = 3 min after sternotomy; T6 = before aortic cannulation.

<table>
<thead>
<tr>
<th></th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
<th>T5</th>
<th>T6</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beat min⁻¹)</td>
<td>62 ±12</td>
<td>62 ±10</td>
<td>64 ±10</td>
<td>57 ±8</td>
<td>59 ±8</td>
<td>65 ±14</td>
</tr>
<tr>
<td>APSyst (mm Hg)</td>
<td>142 ±24</td>
<td>102 ±10*</td>
<td>106 ±14*</td>
<td>115 ±16*</td>
<td>114 ±12*</td>
<td>101 ±17*</td>
</tr>
<tr>
<td>APDiast (mm Hg)</td>
<td>64 ±10</td>
<td>49 ±5*</td>
<td>50 ±7*</td>
<td>60 ±10</td>
<td>62 ±11</td>
<td>55 ±11*</td>
</tr>
<tr>
<td>SVR (dyn s cm⁻⁵)</td>
<td>1037 ±221</td>
<td>773 ±112*</td>
<td>802 ±150*</td>
<td>1138 ±304*</td>
<td>1225 ±370*</td>
<td>1042 ±393</td>
</tr>
<tr>
<td>PPsyst (mm Hg)</td>
<td>28 ±8</td>
<td>25 ±6</td>
<td>26 ±7</td>
<td>25 ±6</td>
<td>24 ±8</td>
<td>20 ±5*</td>
</tr>
<tr>
<td>PpDiast (mm Hg)</td>
<td>13 ±5</td>
<td>11 ±4</td>
<td>10 ±4*</td>
<td>10 ±3*</td>
<td>10 ±5*</td>
<td>8 ±3*</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>13 ±4</td>
<td>13 ±4</td>
<td>12 ±4</td>
<td>13 ±4</td>
<td>12 ±4</td>
<td>10 ±4</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>6 ±3</td>
<td>6 ±4</td>
<td>5 ±4</td>
<td>6 ±3</td>
<td>6 ±3</td>
<td>5 ±3</td>
</tr>
<tr>
<td>CI (litre min⁻¹)</td>
<td>3.6 ±0.7</td>
<td>3.4 ±0.5</td>
<td>3.4 ±0.6</td>
<td>2.9 ±0.6*</td>
<td>2.8 ±0.7*</td>
<td>2.9 ±0.7*</td>
</tr>
<tr>
<td>LVSWI (g m²⁻¹)</td>
<td>62 ±17</td>
<td>42 ±10*</td>
<td>42 ±10*</td>
<td>40 ±11*</td>
<td>45 ±13*</td>
<td>38 ±12*</td>
</tr>
</tbody>
</table>

Pressure of 50 mm Hg. In order to keep mean perfusion pressure constant, either phenylephrine or an infusion of propofol was used to control systemic vascular resistance, when necessary. St Thomas' Hospital cardioplegic solution (1000 ml at 4 °C) and topical cooling of the myocardium were used for myocardial protection.

The infusion of propofol was discontinued at the end of CPB. Fentanyl 0.010 mg kg⁻¹, was given after weaning from CPB.

Results were analysed for statistical significance using analysis of variance. The null hypothesis was rejected if P < 0.05. Where appropriate, analysis of variance was followed by the Walker Duncan Adaptive Procedure. Significance was accepted when P < 0.05.

**RESULTS**

The results are summarized in table II.

**Induction**

Induction of anaesthesia was associated with significant (P < 0.05) decreases in systolic (−28%) and diastolic (−23%) pressures, systemic vascular resistance (−25%) and left ventricular stroke work index (−32%). The decrease in systemic vascular resistance was not associated with an increase in cardiac index or heart rate. Left and right filling pressures were not affected by induction with propofol.

**Maintenance**

The mean infusion rate was 5.15 mg kg⁻¹ h⁻¹ (range 4.05–8.82 mg kg⁻¹ h⁻¹). When haemodynamic data before, and 3 min after, intubation were compared, no significant differences were found for the observed and calculated variables, except for an increase in systemic vascular resistance (P < 0.05). During intubation, however, systolic and diastolic arterial pressures increased in eight of the 15 patients (+26% and +28%, respectively). However, in all these patients the peak systolic arterial pressure at intubation was still less than the awake value. The increase in arterial pressure was transient; vasodilator therapy was not required and the change in pressure was not accompanied by an increase in heart rate.

When haemodynamic data before, and 3 min after, sternotomy were compared, no significant difference could be observed, except for an increase in systemic vascular resistance. In 12 of the 15 patients (80%), arterial pressure remained constant during sternotomy and sternal spread. In two patients there were moderate, but transient,
increases in systolic and diastolic arterial pressures, with peak systolic pressure lower than the awake value. In one patient, sternotomy and sternal spread were associated with a hypertensive reaction (peak systolic pressure 188 mm Hg), but this was easily corrected with nitroglycerin (infused at a rate of 1.5 μg kg⁻¹ min⁻¹).

The significant decrease in left ventricular stroke work index after induction remained significant during maintenance (P < 0.05). Left and right filling pressures were constant during maintenance.

Systemic vascular resistance increased continuously during maintenance; this effect was most pronounced in the period after intubation but before sternotomy. The increase in systemic vascular resistance was associated with a decrease in cardiac index (P < 0.05).

During the maintenance of anaesthesia, systolic arterial pressure remained less than the awake value (P < 0.05).

**Bypass and post-bypass period**

Mean duration of CPB was 107 min ± 32 (SD). Mean aortic cross clamping time was 65 min ± 22. Saphenous aorta–coronary bypass graftings ranged from one to five (mean three) distal anastomoses. In addition, in 13 of the 15 patients the left internal mammary artery was used for an end-to-side anastomosis with the LAD (left anterior descending coronary artery). In three of these patients a proximal stenosis in a diagonal branch of the LAD was bypassed with a side-to-side anastomosis between the left internal mammary artery and the diagonal branch.

Mean propofol infusion rate during CPB was 2.57 mg kg⁻¹ h⁻¹ (range 0–8.41 mg kg h⁻¹). Increments of phenylephrine 1 mg were given in 11 patients, with a maximum dose of 5 mg, especially during the first minutes of CPB, in order to maintain the perfusion pressure at 50 mm Hg.

Weaning from CPB, after rewarming to a rectal temperature of 35 °C, was straightforward in 14 patients. All these patients had a normal (sinus) cardiac rhythm at the end of CPB; they came of bypass with normal left and right filling pressures, without inotropic support, except for calcium chloride 1 g. One patient with a third-degree AV block needed ventricular pacing as well as a high preload before coming off CPB.

Fifteen minutes after the patients were weaned from CPB, systolic and diastolic arterial pressures were 106 mm Hg ± 14 (SD) and 58 mm Hg ± 8. Mean heart rate was 83 beat min⁻¹ ± 9. Mean cardiac index was 3.5 litre min⁻¹ m⁻² ± 0.8 and calculated mean systemic vascular resistance was 810 dyn s cm⁻⁵ ± 195. Mean pulmonary capillary wedge pressure was 15 mm Hg ± 4.

ST-depression, increases in pulmonary capillary wedge pressure or prominent PCWP v-wave, were not observed during anaesthesia and surgery. After surgery, the concentrations of cardiac enzymes (CK, CK-MB, LDH, ASAT, ALAT) were within normal limits in all patients. Postoperative ECG morphology was identical to preoperative ECG morphology in all patients.

**DISCUSSION**

Maintenance of an adequate myocardial oxygen balance is essential during coronary artery bypass surgery. An increase in cardiac work implies a risk that myocardial oxygen demand could exceed supply, distal to the coronary stenosis. This may result in ischaemia or even infarction. An imbalance between supply and demand may be prevented by an anaesthetic technique which causes myocardial depression or assures complete absence of any hypertensive response to noxious stimuli such as intubation and sternotomy. High-dose fentanyl anaesthesia is usually chosen for its minimal effects on cardiovascular dynamics, but the frequency of break-through hypertension is, in our opinion, unacceptably high (de Lange et al., 1982; Sebe et al., 1982; Wynands et al., 1983). Until now, intentional myocardial depression has involved the use of volatile anaesthetics (Moffitt and Sethna, 1986).

It can be concluded from the decrease in left ventricular stroke work index, with no change in atrial filling pressures, that propofol–fentanyl anaesthesia has myocardial depressive properties. Furthermore, the fact that the significant decrease in systemic vascular resistance after induction and intubation was not associated with an increase in cardiac index supports the thesis of a depressed myocardial pump function.

The reduction in arterial systolic and diastolic pressures observed on induction is comparable to the results of other authors who studied propofol as an induction agent in patients with coronary artery disease (Al-Khudhairi et al., 1982; Patrick et al., 1985). In the study by Patrick and colleagues (1985), systolic arterial pressure decreased below 100 mm Hg in eight of the 10 patients after...
induction with propofol 1.5 mg kg⁻¹. In two patients it decreased to less than 70 mm Hg. In our group only five of 15 patients had a systolic arterial pressure less than 100 mm Hg after induction, the lowest arterial pressure observed being 88 mm Hg. This difference was probably the result of the greater left and right filling pressures before induction in our group. Mean pulmonary capillary wedge pressure in our patients was 13 mm Hg, whereas it was 6.6 mm Hg in the patients studied by Patrick and colleagues (1985).

The significant decrease in diastolic arterial pressure on induction and during intubation must result in a decrease in coronary perfusion. This is counterbalanced by a reduction in oxygen demand: systolic arterial pressure is decreased, when compared with the awake value, and myocardial function is depressed in the presence of a reduced afterload. Therefore, it may be concluded that during induction and intubation the heart is not more at risk of ischaemia than before induction. This is supported by the absence of ST-depression, or increased pulmonary capillary wedge pressure.

One patient became hypertensive during sternotomy and sternal spread, and required an infusion of nitroglycerin to control the arterial pressure. A higher incidence has often been recorded during high-dose fentanyl anaesthesia in patients with good left ventricular function, taking beta-adrenoreceptor antagonists. Moffitt and co-workers (1984) reported that two out of 10 patients needed sodium nitroprusside after sternotomy. Waller and associates (1981) reported that eight out of 12 patients required additional anaesthetic drugs and an infusion of nitroglycerin to control hypertension. Sonntag and colleagues (1982) recorded a systolic arterial pressure of more than 200 mm Hg in four out of nine patients after sternotomy. Edde (1981) studied the haemodynamic changes before, and after, sternotomy in patients anaesthetized with fentanyl 50 µg kg⁻¹ given at induction as a single i.v. bolus. All the patients, most of whom were taking beta-adrenoreceptor antagonists, became hypertensive after sternotomy and required vasodilator treatment.

The degree of beta-adrenergic blockade during anaesthesia influences the likelihood of hypertension during intubation, skin incision, sternotomy and sternal spread (de Lange et al., 1982; Moffitt et al., 1984). Our patients received their normal dose of beta-blocking drug up to the day of surgery.

The decreases in diastolic and mean arterial pressures during induction and early maintenance caused a decrease in coronary blood flow. However, myocardial oxygen demand seemed to decrease more than the decrease in oxygen supply, since there was neither ST-depression nor an increase in pulmonary capillary wedge pressure. However, we must consider that, even in the absence of ST-depression, the heart can become ischaemic and produce lactate (Moffitt et al., 1986). The adequacy of myocardial oxygen balance can also be assessed by the endocardial viability ratio (Hoffman and Buckberg, 1978) but this ratio must be used with caution in patients with coronary artery disease. In myocardial regions supplied by a stenotic coronary artery, the critical endocardial viability ratio may increase to an unknown extent. This limitation still exists when more sophisticated techniques are used to assess myocardial metabolism, such as coronary sinus catheterization. Even when supraselective coronary sinus blood sampling is performed, one cannot state with absolute certainty that segmental ischaemia will always be detected (Sethna and Moffitt, 1986).

If periods of regional myocardial ischaemia did occur during induction and maintenance, they were not associated with ST-depression or increases in capillary wedge pressure. Although it may not be stated that the heart was never at risk during the procedure, there was no evidence of myocardial infarction.

Postoperative ECG morphology was unchanged and all the concentrations of the cardiac enzymes were normal.

In conclusion, this study demonstrated that propofol-fentanyl anaesthesia was an adequate technique for coronary bypass surgery in patients with good left ventricular function taking beta-adrenoreceptor antagonists. Myocardial depression was associated with a low incidence of hypertensive reactions to noxious stimuli. Clinical signs of ischaemia were not observed and peroperative infarction did not occur.

ACKNOWLEDGEMENTS

Our thanks are due to ICI Pharmaceutical Division for the supply of propofol.
REFERENCES


