Haemodynamic effects of propofol vs thiopental in infants: an echocardiographic study

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Rapid i.v. induction of general anaesthesia is indicated in infants at risk of vomiting or regurgitation to reduce the risk of aspiration of gastric contents. Propofol is an alternative to thiopental in infants, and we have compared cardiovascular changes when propofol or thiopental was used for induction of anaesthesia in infants. Twenty infants, ASA I or II, aged 1–11 months, undergoing elective surgery were allocated randomly to receive either thiopental or propofol for i.v. induction. Cardiovascular and echocardiographic data were recorded in both groups before, during and for 5 min after induction of anaesthesia. Doses required to induce anaesthesia in each group were mean 10.3 (± 0.9) mg kg⁻¹ of thiopental and 6.1 (± 0.6) mg kg⁻¹ of propofol. Thiopental did not alter significantly systolic or mean arterial pressure, afterload indices, rate-corrected velocity of circumferential fibre shortening or cardiac index, but decreased shortening fraction at 1 and 5 min after induction compared with awake values. Propofol did not alter heart rate, shortening fraction, rate-corrected velocity of circumferential fibre shortening or cardiac index at 1 and 5 min after i.v. induction compared with awake values. After induction, systolic and mean arterial pressures and afterload indices decreased more after propofol than after thiopental. Myocardial contractility decreased significantly 5 min after induction with both agents, but did not become abnormal. Thus propofol decreased arterial pressure more than thiopental because of an effect on afterload. Cardiac output remained unchanged with both agents.


Keywords: anaesthetics i.v., propofol; anaesthetics i.v., thiopental; heart, myocardial function; measurement techniques, echocardiography; anaesthesia, paediatric

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Rapid i.v. induction of general anaesthesia is indicated in infants at risk of vomiting or regurgitation to reduce the risk of aspiration of gastric contents. Thiopental is used frequently in paediatric anaesthesia, but propofol seems to be a good alternative. Indeed, propofol has been used in paediatric anaesthesia since 1985 and has advantages such as rapid induction and recovery time. The cardiovascular effects of propofol have been reported in children, but few data are available in infants. We have compared the cardiovascular changes when propofol or thiopental was used for induction of anaesthesia in infants.

Patients and methods

After obtaining approval from the Local Human Studies Committee and informed written parental consent, we studied 20 ASA I or II infants requiring elective surgery. The age limit for inclusion was 1–12 months. Infants were premedicated 30 min before induction of anaesthesia with midazolam 0.3 mg kg⁻¹ rectally and fasted for 4 h before operation. Infants were allocated randomly by computer listing to receive thiopental or propofol for induction of anaesthesia. After placement of an i.v. cannula and preoxygenation, i.v. induction was performed with either propofol 2 mg kg⁻¹ or thiopental 5 mg kg⁻¹ injected over 10 s. Further induction agent was given after waiting for 10 s until the infant was able to tolerate the face mask. Thus for each agent, a second dose was given at a rate of 0.2 mg kg⁻¹ s⁻¹ for 10 s. Further induction agent was then given if required at a rate of 0.1 mg kg⁻¹ s⁻¹ until the face mask could be tolerated. The total dose of drug used was recorded. Measurements were made after induction (T1) and 5 min later (T1+5), without using other anaesthetic agents, during spontaneous ventilation breathing oxygen.

At each time, the following measurements were recorded by the same observer blinded to the agent that had been
used: heart rate (beat min$^{-1}$), arterial pressure (mm Hg), measured using an automated arterial pressure cuff, and continuous Doppler and two-dimensional transthoracic echocardiographic data (Hewlett Packard Sonos 1000, Andover, MA, USA). The echocardiographic data obtained in each patient included measurement of aortic diameter and shortening fraction. In the long axis view of the left ventricular outflow tract (using M mode), the end-systolic internal aortic annular diameter ($\Omega_{Ao}$) was measured, and aortic sectional area ($S_{Ao}$) calculated ($S_{Ao}=\pi(\Omega_{Ao})^2/4$). Shortening fraction (SF) was measured by M mode from the parasternal long axis view of the left ventricle at the junction of the mitral valve leaflets and papillary muscle. Left ventricular end-diastolic diameter (LVDD) was measured at the point of maximal diameter and left ventricular end-systolic diameter (LVSD) at the point of peak upward deflection of the posterior wall. Posterior wall thickness ($P_{Wes}$) was measured at end-systole. SF was calculated by ($LVDD-LVSD$)/$LVDD$ and expressed as a percentage. Rate-corrected velocity of circumferential fibre shortening (VCFc) was calculated using the formula: $VCFc=SF$\text{rate-corrected ejection time}. Rate-corrected ejection time=$\text{ejection time divided by the square root of the R–R interval (to correct to a heart rate of 60 beat min$^{-1}$)}$. Left ventricular end-systolic wall stress (ESWS) was calculated using the formula:

$$ESWS = \frac{(1.35 \times MAP \times LVSD)}{((1+P_{Wes}/LVSD) \times (P_{Wes}) \times 4)}.$$ 

As described previously,$^6$ VCFc–ESWS or SF–ESWS relationships were calculated to determine contractility independent of loading conditions.$^7$ The normal value of z score was $-2$ to $+2$.

Continuous Doppler was used to measure flow in the ascending aorta by the suprasternal approach. Continuous Doppler studies were performed with the same scanner as above using 5-MHz transducers with Duplex imaging. The combination of audio signal intensity, spectral display and simultaneous imaging was used to confirm positioning for maximal aortic blood flow velocities. Because the angle between estimated direction of blood flow and Doppler beam was 15° or less, no angle correction of the Doppler signal was made. Mean aortic flow velocity ($V_{ao}$) was calculated by the software of the ultrasound system as average velocity$\times$flow period. The average of three consecutive flow velocity integrals was obtained. Cardiac index (CI) was calculated from the volumetric equation:

$$CI (ml kg^{-1} min^{-1}) = V_{ao} (cm s^{-1}) \times S_{Ao} (cm^2) \times \frac{60}{body weight (kg)}.$$ 

Systemic vascular resistance (SVR) was evaluated as the quotient of mean arterial pressure and CI without measurements of right atrial pressure. All echocardiographic data were calculated again by a second observer in a blinded fashion. Continuous data, parametrically distributed between groups, were analysed using the Mann–Whitney test. The Kruskal–Wallis test was used to compare two groups with multiple treatments within groups, and a Wilcoxon test was used for multiple treatments within the same group. A probability value less than 0.05 was considered significant. Calculation was performed with the BI LOGINSERM 1979/1987 software. Values are expressed as mean (SD).

### Results

We studied 20 infants: 10 received thiopental and 10 propofol. The groups were comparable in age (4.8 (range 1–8) months and 6.2 (range 1–11) months for the thiopental and propofol groups, respectively), sex distribution and weight (mean 6.5 (SD 1.6) kg for thiopental and 6.9 (2.1) kg for propofol). Groups were also comparable in baseline values of cardiovascular measurements (Figs 1, 2; Table 1).

Doses required to induce anaesthesia in each group were 10.3 (0.9) mg kg$^{-1}$ for thiopental and 6.1 (0.6) mg kg$^{-1}$ for propofol.

**Cardiovascular effects of thiopental**

Thiopental did not significantly alter systolic (SAP) or mean (MAP) arterial pressures, LVDD, VCFc, SVR, ESWS (Table 1) or CI (Fig. 1) during induction of anaesthesia compared with awake values. Thiopental decreased significantly SF during induction. Stress–velocity index (SVI) or VCFc–ESWS relationship, and the stress–shortening index (SSI) or SF–ESWS relationship, were also decreased significantly but did not fall into the abnormal range (Fig. 2).

**Cardiovascular effects of propofol**

Propofol did not alter HR, LVDD, SF, VCFc (Table 1) or CI (Fig. 1) during induction of anaesthesia compared with awake values. Propofol decreased significantly SAP, MAP, ESWS and SVR during induction compared with awake values. SVI and SSI decreased significantly but did not fall into the abnormal range (Fig. 2).

**Cardiovascular effects of propofol compared with thiopental**

Comparing the propofol and thiopental groups, propofol caused a greater decrease in SAP, MAP, SVR and ESWS than thiopental (Table 1). However, there was no significant difference in LVDD, SF, VCFc, SSI, SVI or CI (Figs 1, 2; Table 1).

### Discussion

Arterial pressure is an important variable used to assess haemodynamic conditions in children. However, examination of the two determinants of arterial pressure (cardiac output and peripheral vascular resistance) is needed to assess the possible different effects of the anaesthetics. In this study, arterial pressure decreased more in the propofol
group compared with the thiopental group, with no significant change in left ventricular cardiac output.

**Induction dose required in infants**

Before comparing the effects of the two agents, the total dose used for induction should be considered. The larger central compartment and greater clearance explain the increased requirements of propofol for induction of anaesthesia in young compared with older children. The dose of propofol required to induce anaesthesia in 50% (ED$_{50}$) or 90% (ED$_{90}$) of healthy children has been determined in several studies. Two methods were used to assess depth of anaesthesia in children: loss of eyelash reflex and acceptance of a face mask, corresponding respectively to a lighter level or slightly deeper level of anaesthesia.

Acceptance of a face mask is more clinically relevant than loss of eyelash reflex and was used in this study to assess depth of anaesthesia during induction. Aun and colleagues reported that values for ED$_{50}$ and ED$_{90}$ were higher in young (<2 yr) than in older children. Similarly, the ED$_{50}$ in unpremedicated infants was set at approximately 3.0 mg kg$^{-1}$ by Westrin. However, the ED$_{90}$ is more relevant clinically than the ED$_{50}$, but the ED$_{90}$ of propofol is not yet known in infants. In studies performed in children, the ED$_{90}$ was twice that of the ED$_{50}$. Thus while the doses of propofol used for induction in this study were greater than the ED$_{90}$ as reported by others in children, they were approximately twice the ED$_{50}$ reported in infants and could correspond to an ED$_{90}$ in infants. In contrast, the ED$_{50}$ and ED$_{90}$ for thiopental have been determined by Brett and Fisher in infants, and were 4.1 mg kg$^{-1}$ and 8.6 mg kg$^{-1}$, respectively. Greater values for ED$_{50}$ were reported by Westrin (6.3 mg kg$^{-1}$) and by Jonmarker and colleagues (7.5 mg kg$^{-1}$). Thus, as with propofol, the doses of thiopental used in this study appear to be similar to ED$_{90}$ values reported by others.

An equipotent dose is needed to compare the haemodynamic effects of both agents. The ratio of thiopental ED$_{50}$ to propofol ED$_{50}$, described in the infant, ranged from 1.43:1 to 2.5:1 and remained unchanged when calculated for ED$_{90}$. Edelist found a similar ratio of 1.6:1 for propofol and thiopental given as a bolus injection in adults. Thus the 1.7:1 ratio of induction doses used in each infant group in this study was similar to those reported by others.

**Effects of thiopental and propofol on arterial pressure**

Propofol decreases arterial pressure after induction in children by approximately 5–25%. However, in younger children, a slight decrease in mean arterial pressure of similar magnitude was demonstrated with both propofol and thiopental. During rapid induction in infants, less hypertension after induction was found with propofol compared with thiopental, but no decrease in systolic arterial pressure was demonstrated. Therefore, while haemodynamic effects in these three studies were less than reported by others in older children or in adults, the doses used corresponded to only the ED$_{50}$ for each agent. Using a greater dose in infants, Westrin and colleagues reported no decrease in systolic arterial pressure 1 min after thiopental induction.
in infants, but a decrease of approximately 5% after propofol.\textsuperscript{13, 15} We found similar results in this study as SAP decreased by approximately 4% after propofol induction and increased by approximately 4% after thiopental. Westrin and colleagues did not report values for MAP. We found that MAP decreased more than SAP after propofol induction in infants. Indeed, in our study, MAP decreased by approximately 15% after induction, and by more than 25%, 5 min later with propofol. However, this decrease in MAP was similar to that described with sevoflurane (28%) and less than that with halothane (38%) in infants.\textsuperscript{21}

**Effects of thiopental and propofol on cardiac output**

Cardiac output depends on heart rate and stroke volume, and the latter depends on contractility and afterload. Heart rate is one of the main determinants of cardiac output in infants. Murray, Forbes and Mahoney showed that halothane decreases heart rate, stroke volume and cardiac output in infants.\textsuperscript{22} However, heart rate and cardiac output increased without change in stroke volume after administration of atropine 0.02 mg kg\textsuperscript{-1}, showing that cardiac output is in part dependent on heart rate. In our study, heart rate did not change significantly with either agent. Heart rate decreased very little with propofol after induction. Westrin and colleagues found an increase in heart rate in infants 1 min after induction with both thiopental and propofol, but in these studies, patients received atropine i.v. just before induction.\textsuperscript{13, 15} Borgeat and co-workers reported in children a slight decrease in heart rate of approximately 5–10% after propofol and an increase of approximately 8–12% with thiopental, but atropine was given orally 60 min before induction.\textsuperscript{5} In younger children, propofol decreased heart rate more than thiopental after induction.\textsuperscript{19} Thiopental and propofol both caused an initial increase in heart rate, which stabilized more rapidly after propofol.\textsuperscript{4} Only one study reported a greater decrease in heart rate (24%) after induction with propofol compared with thiopental (11%) in younger children.\textsuperscript{23} However, 0.5% halothane and 70% nitrous oxide immediately after induction could affect heart rate. Several studies have reported that halothane decreased heart rate in infants.\textsuperscript{4, 6, 22, 24}

Stoke volume is the second factor that influences cardiac output, but few studies have been performed in infants during anaesthesia. Stroke volume depends on both contractility and afterload. Shortening fraction decreased slightly or remained unchanged when both contractility and afterload decreased simultaneously.\textsuperscript{5} In our study, SF and VCFc did not change after induction with propofol, as shown previously by Aun and colleagues\textsuperscript{23} Using indices of contractility independent of loading conditions (SVI and SSI), we have shown that the decrease in contractility was similar with both thiopental and propofol in infants. However, the greater decrease in afterload in the propofol group leads to maintained shortening fraction, unlike thiopental. Thus slight effects on heart rate and contractility explain why no relevant change in cardiac output was seen in either group, in contrast with changes reported by Aun and colleagues. The decrease in cardiac output reported by these authors was caused by a decrease in heart rate in the propofol group, and interactions between halothane, nitrous oxide and i.v. agents cannot be ruled out.\textsuperscript{23}

**Effects of thiopental and propofol on afterload**

A decrease in afterload with propofol has been reported in several studies in adults,\textsuperscript{25–29} mediated by inhibition of sympathetic vasoconstrictor activity and impairment of baroreflex regulatory mechanisms.\textsuperscript{30, 31} In our study, afterload decreased by approximately −14% to −27% after propofol but remained unchanged after thiopental. Similar results were reported in adults.\textsuperscript{27, 28} Indeed, Gauss, Heinrich and Wilder-Smith reported that propofol induced simultaneous negative inotropic effects and reduction in afterload, while thiopental had exclusively negative inotropic effects.\textsuperscript{28} Similarly, Price and colleagues reported a significant

<table>
<thead>
<tr>
<th>Group</th>
<th>Awake</th>
<th>T1</th>
<th>T1 + 5</th>
<th>(T vs P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beat min\textsuperscript{-1})</td>
<td>T</td>
<td>139 (20)</td>
<td>144 (21)</td>
<td>135 (20)</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>141 (23)</td>
<td>131 (15)</td>
<td>130 (17)</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>T</td>
<td>114 (15)</td>
<td>105 (10)</td>
<td>93 (10)*</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>109 (15)</td>
<td>105 (10)</td>
<td>93 (10)*</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>T</td>
<td>79 (14)</td>
<td>89 (12)</td>
<td>72 (17)</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>80 (19)</td>
<td>86 (9)</td>
<td>58 (6)*</td>
</tr>
<tr>
<td>LVDD (cm)</td>
<td>T</td>
<td>2.4 (0.2)</td>
<td>2.4 (0.2)</td>
<td>2.0 (0.2)</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>2.4 (0.3)</td>
<td>2.5 (0.2)</td>
<td>2.4 (0.2)</td>
</tr>
<tr>
<td>SF (%)</td>
<td>T</td>
<td>38 (6)</td>
<td>32 (4)*</td>
<td>33 (6)*</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>36 (4)</td>
<td>35 (6)</td>
<td>35 (3)</td>
</tr>
<tr>
<td>VCFc (circ s\textsuperscript{-1})</td>
<td>T</td>
<td>1.03 (0.20)</td>
<td>0.81 (0.12)</td>
<td>0.87 (0.18)</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>0.94 (0.14)</td>
<td>0.89 (0.21)</td>
<td>0.91 (0.10)</td>
</tr>
<tr>
<td>ESWS (g cm\textsuperscript{-2})</td>
<td>T</td>
<td>40.5 (10.2)</td>
<td>53.9 (18.5)</td>
<td>42.4 (10.6)</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>47.9 (21.0)</td>
<td>40.0 (12.0)</td>
<td>32.0 (5.1)*</td>
</tr>
<tr>
<td>SVR (dyn s cm\textsuperscript{-5})</td>
<td>T</td>
<td>1282 (238)</td>
<td>1449 (319)</td>
<td>1250 (299)</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>1366 (385)</td>
<td>1171 (273)</td>
<td>1001 (166)*</td>
</tr>
</tbody>
</table>
decrease in systemic vascular resistance by approximately -23% after propofol but not with thiopental.22

In summary, in healthy infants, propofol decreased mean arterial pressure more than thiopental, without change in cardiac output. Decrease in afterload, rather than decrease in contractility or heart rate, appeared to be the main factor in the decrease in arterial pressure in infants. Propofol is an alternative to thiopental for i.v. induction in infants older than 1 month, without greater adverse haemodynamic effects, but caution may be needed when propofol is used in non-elective cases in infants that may not be adequately hydrated.

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