Thiopental Requirements for Induction of Anesthesia in Neonates and in Infants One to Six Months of Age

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The authors determined the thiopental dose needed for satisfactory induction in ten neonates, 0–14 days of age, and 20 infants, 1–6 months of age. A single iv bolus of thiopental was given. Thirty seconds after injection the anesthesia mask was applied and the response was observed during the following 30 s while the patient breathed oxygen. Induction was considered satisfactory if there were no gross movements or coughing. The dose required for satisfactory induction in 50% of patients, ED₅₀ (± SE), was 3.4 ± 0.2 mg/kg in neonates and 6.3 ± 0.7 mg/kg in infants (P < 0.001). It is concluded that the thiopental dose needed for satisfactory induction is less in neonates than in infants. (Key words: Anesthesia: pediatric. Anesthetics, intravenous: thiopental.)

In a previous study we found that the thiopental dose (mg/kg) needed for “satisfactory” induction of anesthesia was greater in infants than in children. The median effective dose in infants 1–6 months of age was 6.9 mg/kg. Neonates were not included in the study, but it has been our impression, and that of others, that they usually need smaller doses. In the present study the thiopental doses needed for induction in neonates and in infants were compared.

Methods

Ten neonates, 0–14 days of age, and 20 infants, 1–6 months of age, were studied. The patients were ASA physical status 1 or 2, born at full term (>37 weeks gestational age) and with a birthweight greater than 2,500 g. All had normal body temperatures, no signs of upper respiratory tract infection, and were scheduled for non-emergency surgery not requiring rapid sequence induction. Typical procedures included hernia repair in infants and surgery for anal atresia in neonates. Some demographic data are shown in Table 1. The study was approved by the local Human Ethics Committee.

The children were kept fasting for at least four hours preoperatively. Preanesthetic medication was not given. An iv catheter (24-G) was inserted in the hand or in the antecubital fossa on the ward before transport to the operating room. Monitoring included ECG, blood pressure, and oxygen saturation measured with a Nellcor® pulse oximeter (SpO₂).

Anesthesia was induced in a standardized manner. Atropine (0.1 mg) was given iv. Oxygen was flushed over the face for 1 min while the anesthesia mask was held 1–2 cm from the patient. A precalculated dose of 2.5% thiopental was then given as an iv bolus over approximately 5 s followed by 2–3 ml of saline. All iv drugs were given through a three-way stopcock. ED₅₀ was obtained by the “up and down method.” The procedure was as follows. The first patient in each age group was given 3.2 mg/kg of thiopental (=10.5 mg/kg). Thirty seconds after injection the child’s chin was gently moved into the sniffing position and the anesthesia mask was placed over the face. Care was taken to avoid painful stimulation when lifting the chin and while holding the anesthesia mask. The response during the following 30 s of oxygen breathing was judged by an observer unaware of the administered dose. If the child coughed, moved head or trunk, or lifted an elbow or foot from the table during the following 30 s, induction was classified as unsatisfactory and additional thiopental was given as needed. The dose chosen for the next patient in that age group was then increased by 25%. If the patient did not move, or only showed minor movements of a hand or foot, induction was classified as satisfactory, and a 20% smaller thiopental dose was selected for the subsequent patient. The doses were thus spaced evenly on a logarithmic scale (fig. 1).

Systolic blood pressure, heart rate, and SpO₂ were measured just before and 1 min after the thiopental bolus. The blood pressure was obtained with an inflatable cuff and a mercury manometer, using a Doppler probe or the pulse oximeter as pulse indicator. At the end of the observation period, i.e., 60 s after the thiopental bolus, 2 mg/kg of succinylcholine was given, the trachea was intubated, and general anesthesia was established with halothane in N₂O/O₂.

ED₅₀ was calculated as described by Dixon. The method allows estimation of ED₅₀ from a relatively small sample size and has previously been used to assess halothane and isoflurane MAC. To determine the SE of the estimated ED₅₀ in the age group, ED₅₀ was determined in subgroups of consecutively studied patients, each with a “nominal sample size” of 2. (The nominal sample size is a count of the number of patients, beginning with the first pair of patients with unlike responses. A run of, e.g., unsatisfactory-unsatisfactory-satisfactory has a nominal
TABLE 1. Patients

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>N</th>
<th>Age (days)</th>
<th>Weight (kg)</th>
<th>Length (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–14 days</td>
<td>10</td>
<td>4 ± 1</td>
<td>3.5 ± 0.2</td>
<td>51 ± 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0–14)</td>
<td>(2.9–4.5)</td>
<td>(48–55)</td>
</tr>
<tr>
<td>1–6 months</td>
<td>20</td>
<td>92 ± 9</td>
<td>5.8 ± 0.3</td>
<td>62 ± 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(37–156)</td>
<td>(4.0–8.3)</td>
<td>(52–72)</td>
</tr>
</tbody>
</table>

Values are given as mean ± SEM. Values within parentheses indicate ranges.

Results

ED$_{50}$ (± SE) was 3.4 ± 0.2 mg/kg in neonates and 6.3 ± 0.7 mg/kg in infants ($P < 0.001$). The individual responses in each group are shown in figure 1. The combined results of the present and previous study are depicted in figure 2. ED$_{50}$ in infants was not significantly different from the value previously observed in the same age group.$^{1}$

No child coughed, but five neonates and ten infants moved in response to the anesthesia mask and were therefore given additional thiopental. The movements prohibited a full series of blood pressure, heart rate, and SpO$_2$ measurements in six patients. No child developed bradycardia or hypotension (table 2). SpO$_2$ was greater than 94% in all children, and no patient needed ventilatory assistance during the 60 s between thiopental and succinylcholine injections.

Discussion

In the present study, the mask was applied 30 s after thiopental injection, and not after 40 s as in the previous study.$^{1}$ This was because a short arm–brain circulation time was expected in the small patients of the present study. However, ED$_{50}$ in infants 1–6 months of age was not significantly different in the two studies (fig. 2). Obviously, the dose needed for satisfactory induction of anesthesia depends on what criteria of satisfactory induction are used. In adults, loss of the lid reflex is commonly used to assess whether the patient is asleep or not. We did not include testing of the lid reflex in the present study because it was difficult to do in some neonates due to postpartum edema of the eyelids. Also, the disappearance of the lid reflex does not necessarily imply that induction is satisfactory. In our previous study, we found that 35% of children who had a negative lid reflex coughed or moved when the anesthesia mask was applied.$^{1}$

In young children the criteria used in the present study,
Table 2. Heart Rate and Blood Pressure during Induction

<table>
<thead>
<tr>
<th>Age Group</th>
<th>N</th>
<th>Thiopental Dose* (mg/kg)</th>
<th>Blood Pressure (mmHg) Before Induction</th>
<th>Heart Rate (beats/min) Before Induction</th>
<th>1 min after Induction</th>
<th>1 min after Induction</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–14 days</td>
<td>7</td>
<td>5.4 ± 0.8</td>
<td>77 ± 7 (50–100)</td>
<td>144 ± 3 (115–150)</td>
<td>77 ± 6 (60–100)</td>
<td>155 ± 4 (120–170)</td>
</tr>
<tr>
<td>1–6 months</td>
<td>17</td>
<td>7.9 ± 0.5</td>
<td>102 ± 5 (75–150)</td>
<td>159 ± 6 (120–210)</td>
<td>102 ± 6 (60–170)</td>
<td>172 ± 4† (151–200)</td>
</tr>
</tbody>
</table>

* The thiopental dose includes supplementary doses given to children who did not fall asleep after the initial doses. Values are given as mean ± SEM. Values within parentheses indicate ranges.
† Significant change in relation to preinduction value (P < 0.05).

Thiopental in blood may be greater in neonates than in infants. This is suggested by the findings of Kingston et al. who reported a free fraction of 15–24% in umbilical cord blood, and those of Sorbo et al. who observed a free fraction of 13 ± 2% (mean ± SD) in young children. Second, blood–brain equilibrium may occur faster in neonates because of a more permeable blood–brain barrier. Finally, the brain concentration that is needed for sleep may be less in neonates. This may be because of anatomic differences, because neither dendrite development nor synaptogenesis is complete at birth, or because of increased hormone levels, e.g., of progesterone.

We observed no adverse cardiovascular changes during induction. However, the present study was not primarily designed to assess the circulatory effects of thiopental induction. Thus, we followed our usual practice of giving infants below 10 kg of weight a standard dose of 0.1 mg of atropine. If atropine is not given, a decrease in blood pressure may occur. Tibballs and Malbezir gave 7.5–8.5 mg/kg of thiopental to infants 2–12 months of age, and observed a 25% decrease in cardiac index and a 16% decrease in blood pressure immediately before tracheal intubation.

Although thiopental is well tolerated in healthy infants, it may not be an ideal agent in very young individuals. The anesthetic effect is largely determined by redistribution, but one cannot exclude the possibility that a slow final elimination may delay recovery in that age group. The hepatic metabolic pathways are less well developed, and thiopental given before caesarean section has considerably longer terminal half-life in newborns than in their mothers.

In summary, we found that the ED₅₀ for satisfactory induction of anesthesia with thiopental in neonates was about 60% of that in infants.

References