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Faster Recovery after Anesthesia in Infants after Intravenous Induction with Methohexital Instead of Thiopental

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Background: **To determine possible delays in recovery after intravenous anesthesia induction with thiopental, the drug was compared with methohexital in infants 1–12 months of age who were scheduled for hernia repair or circumcision.**

Methods: **The infants were given equipotent doses of methohexital (3.0 mg/kg, n = 21) or thiopental (7.3 mg/kg, n = 20), in random and blind fashion. After tracheal intubation, anesthesia was maintained with isoflurane in nitrous oxide/oxygen. All children received 0.75 ml/kg caudal bupivacaine (2.5 mg/ml). Isoflurane was discontinued at the beginning of skin closure, and nitrous oxide was terminated immediately after the last suture (end of surgery).**

Results: **There were no differences between the two groups with respect to age, weight, or duration of surgery, which lasted 19 min (14–23 min) in the methohexital group and 16 min (15–19 min) in the thiopental group (median and inner quartile range). Time from termination of nitrous oxide to extubation did not differ significantly between the groups. Time to spontaneous eye opening after end of surgery was 23 min (5–44 min) after methohexital induction and 55 min (25–74 min) after thiopental induction ($P < 0.05$). Recovery, assessed as postanesthetic recovery scores by a blinded observer, was significantly more rapid in the methohexital group at arrival in the recovery room and 5, 15, and 45 min after arrival. After 120 min, almost all infants of both groups were awake.**

Conclusions: **Recovery after short surgical procedures in infants is faster after intravenous induction with methohexital than with thiopental. (Key words: Anesthesia: infant; pediatric. Anesthetics, intravenous: methohexital; thiopental. Recovery.)**

THE existence of effective topical anesthesia for venipuncture (*e.g.*, EMLA) makes intravenous anesthesia induction a realistic alternative to mask or rectal induction of anesthesia in children. After intravenous administration of hypnotic agents, the excitatory stage during which the patient is prone to react with laryngospasm in response to stimulation of the upper airway is rapidly passed. This is particularly desirable in small children and infants, whose oxygen reserves are small in relation to their metabolism.[1,2] Furthermore, inserting an intravenous catheter before induction increases safety by facilitating the administration of fluids, muscle relaxants, or anticholinergics.

One conceivable drawback with intravenous induction is that the intravenous agent might have residual effects during the postanesthetic recovery phase. We have believed that thiopental, the most frequently used drug, sometimes causes such problems particularly in young infants. Methohexital dissolved in a lipid emulsion is a possible alternative.[3] The aim of the current study was to assess recovery after anesthesia induced with intravenous methohexital or thiopental in infants 1–12 months of age.

Materials and Methods

After institutional approval and informed consent from the parents, 41 infants between 1 and 12 months of age, scheduled for hernia repair or circumcision, were randomly assigned to receive intravenous induction of anesthesia with methohexital or thiopental. Randomization was stratified according to postnatal age: 1–3, 4–6, and 6–12 months. All children were ASA physical status 1, born full term (>37 weeks' gestational age), with a birth weight greater than 2,500 g. Exclusion criteria were signs of infection, allergy to soybean, surgery lasting longer than 40 min, emergency surgery requiring rapid-sequence induction, and failure to establish venous access. Preoperatively, the child fasted for at least 4 h. No preanesthetic medication was

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Table 1. Postanesthetic Recovery Score

	Score
Consciousness	
Awake	2
Responding to stimuli	1
Not responding	0
Airway	
Coughing or crying	2
Maintaining good airway	1
Airway requires maintenance	0
Movement	
Moving limbs purposefully	2
Nonpurposeful movements	1
Not moving	0

given. After treatment with a local anesthetic ointment (EMLA, Astra Pharmaceuticals), a 24-G catheter was placed in a vein in the hand or antecubital fossa.

The anesthetic induction was performed by an independent anesthesiologist to keep the investigator unaware of the drug used. After injection of 0.005 mg/kg intravenous glycopyrrolate, either 3.0 mg/kg methohexital‡ or 7.3 mg/kg thiopental, *i.e.*, 115% of the respective ED_{50}s in infants aged 1–6 months,[3,4] was given as a bolus injection and flushed with saline. After inducing paralysis with 2 mg/kg succinylcholine, the trachea was intubated, and general anesthesia was continued with isoflurane in nitrous oxide/oxygen (65%/35%). Monitoring included electrocardiogram, blood pressure, pulse oximetry (Nellcor N-100), oxygen saturation, esophageal temperature, and end-tidal carbon dioxide tension (Datex Normocap). An end-tidal carbon dioxide tension about 35 mmHg was maintained. About 10 min before surgery, a caudal block with 0.75 ml/kg bupivacaine (2.5 mg/ml) was performed. Isoflurane was supplied via a calibrated vaporizer at the lowest concentration that kept the child immobile and adequately anesthetized as judged from heart rate, blood pressure, and pupil size. Isoflurane was discontinued 5 min before the expected end of surgery, and the end-tidal carbon dioxide tension was allowed to increase to 40–45 mmHg. Nitrous oxide was stopped when the last suture was tied. After 2 min of oxygen ventilation, transition to spontaneous breathing was attempted. When this was well established and there were age adequate movements, *i.e.*, grimacing and movement of all four extremities in the young infant, and more purposeful movements, *e.g.*, attempts to remove the tube in the older infant, the trachea was extubated. Time from end of surgery to tracheal extubation was noted. The child was transported to the recovery room when it maintained patent airways without assistance and an oxygen saturation greater than 95% breathing room air.

In the recovery room, the child was connected to a pulse oximeter and an HP 78833A unit that recorded chest movements by measuring variations in electric impedance between electrocardiograph electrodes. Postanesthetic recovery (PAR) score (table 1)[5] was determined at arrival and 5, 15, 30, 45, 60, and 120 min after arrival by two specially trained nurses unaware of which induction agent was given. Incidence of pain (scored as none, mild, or severe) and central apnea (defined as absence of chest movements for more than 20 s) was noted, as was time to spontaneous eye opening. Postoperative pain was managed with rectal 15 mg/kg paracetamol.

Unless otherwise stated, the results are expressed as median and inner quartile range. Difference in time to full recovery was assessed by survival analysis with the log-rank test. Comparison of durations and of PAR scores was performed with the Mann-Whitney U-test. $P < 0.05$ was considered to indicate statistical significance.

Results

Twenty-one infants were given methohexital, and 20 received thiopental. The groups were similar with respect to age, weight, length (table 2), and duration of anesthesia and surgery (table 3).

In all children, anesthesia was judged to be satisfactorily induced with the doses given. The maintenance

Table 2. Patient Characteristics

Study group	n	Age (days)	Weight (kg)
Methohexital	21	179 (65–294)	6.8 (4.8–9.0)
Thiopental	20	140 (81–278)	6.6 (4.8–8.7)

Values are median (inner quartile range).

‡ Methohexital, 100 mg, was first dissolved in 1 ml NaCl. When the solution was clear, 9.0 ml of 20% lipid emulsion (Intralipid, Kabi Pharmacia Pharmaceuticals, Sweden) was added to give a 10-mg/ml solution. The solution was used within 2 h.[3]

Table 3. Durations

Group	n	Isoflurane Inhalation (min)	Surgery (min)	Anesthesia Induction until Arrival in the Recovery Room (min)	Termination of N_2O until Extubation (min)	Extubation until Spontaneous Eye Opening (min)
Methohexital	21	41 (30–46)	19 (14–23)	55 (46–61)	5.0 (4–6)	23* (5–44) (n = 17)
Thiopental	20	35 (30–41)	16 (15–19)	51 (48–55)	7.0 (5–10)	55 (25–74) (n = 19)

Values are median (inner quartile range).

* Significant difference between the groups ($P < 0.05$).

isoflurane concentration, *i.e.*, the vaporizer setting about 5 min after skin incision, was 0.75% (0.65–0.75%) in the methohexital group and 0.75% (0.5–1.0%) in the thiopental group. Six patients in the methohexital group and four in the thiopental group needed inspired isoflurane concentrations >1.0% for a few minutes during hernia dissection.

There was no significant difference in time from end of anesthesia to extubation ($P = 0.10$). Spontaneous eye opening occurred significantly earlier after methohexital (table 3). Recovery, assessed with PAR scores, was more rapid after methohexital than after thiopental until the children had been 60 min in the recovery room (fig. 1). Time in the recovery room until a full PAR score was reached was 30 (5–60) and 60 (45–120) min, respectively ($P < 0.005$). At 120 min, one infant in the thiopental group, aged 2.5 months, still had a PAR score of 1.

Pain occurred equally over time in both groups, and there were no differences in pain intensity. The majority of children were scored as having "no pain," but seven in each group were given paracetamol, most of these having "mild pain."

No episode of hypoxemia was noted. One infant given thiopental had repeated apnea episodes during the first 5 min after extubation. No apnea was recorded in the recovery room.

Discussion

The postanesthetic score introduced by Steward was used to assess recovery.[5] The score is well established for assessing wakefulness and return of airway patency. In older children, the time elapsed to specific endpoints—spontaneous eye opening, giving name, and standing unaided—may be used to assess recovery.[6,7] Of these, only spontaneous eye opening was applicable in the current study.

To reduce confounding factors, glycopyrrolate was given as anticholinergic so that central nervous system effects from atropine were avoided.[8,9] In contrast, the use of caudal bupivacaine indirectly may have enhanced sedation by eliminating pain. There was no evidence of a converse effect, with remaining sedation masking pain: the timing and dosing of paracetamol postoperatively was similar in the two groups despite the longer-lasting sedation in infants given thiopental.

Barbiturates are rapidly redistributed from the brain, and when a barbiturate is the sole anesthetic agent and is given as a bolus, unconsciousness only lasts a few minutes. The less rapid progress to complete recovery and longer time to spontaneous eye opening in the thiopental group suggest, however, that rather small plasma concentrations are associated with significant sedation in infants. This agrees with findings in children[10] and in adults[11] in whom central nervous system effects (*e.g.*, drowsiness, respiratory depression) may persist even when the plasma concentration of thiopental is only 1–2% of the initial concentration. In this context, it may be relevant to mention the report by Andropoulos *et al.*[12] of apnea after pyloromyotomy in three full-term infants in whom anesthesia was induced by intravenous thiopental and maintained with halothane/nitrous oxide.

To ensure a satisfactory induction of anesthesia in all children, with equipotent doses of methohexital or thiopental, 115% of previously established ED_{50} doses[3,4] were given. No universally accepted endpoint exists for satisfactory intravenous induction, but these doses conform with those we usually employ in infants

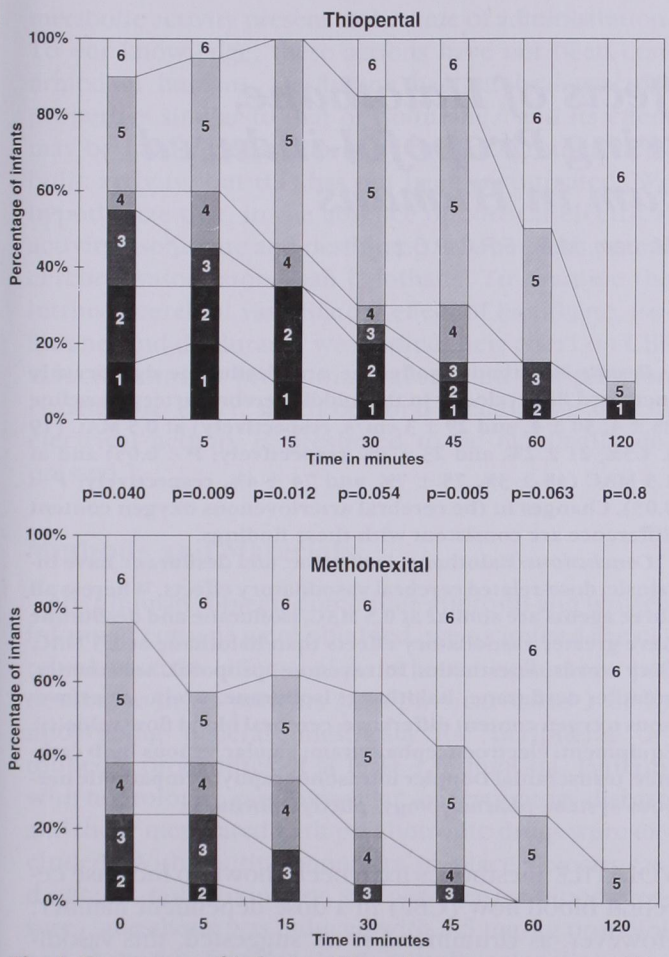

Fig. 1. Percentage of infants with each recovery score at different times after arrival in the recovery room. Recovery scores 1–6 are indicated. There were 21 infants in the methohexital group, and 20 in the thiopental group. The groups were compared with the Mann-Whitney U test. Obtained *P* values are indicated.

older than 1 month. The doses usually give a depth of anesthesia that allows a brief period of ventilation by mask. Thereby, the safety of giving relaxants for intubation can be assessed. In the rarer case that inhalation of volatile anesthetic *via* mask is planned, the dosage ensures smooth transition to inhalational anesthesia in the majority of patients.

In conclusion, recovery after short surgical procedures in infants was more rapid after intravenous induction with methohexital than with thiopental.

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