Recovery after propofol infusion anaesthesia in children: comparison with propofol, thiopentone or halothane induction followed by halothane maintenance

C. S. T. Aun, T. G. Short, M. E. O'Meara, D. H. Y. Leung, Y. M. Rowbottom and T. E. Oh

SUMMARY
We have compared the recovery profiles of 163 healthy Chinese children after general anaesthesia for minor surgical procedures. Patients were allocated randomly to receive one of four anaesthetic techniques: propofol infusion for induction and maintenance using a pharmacokinetic model-controlled syringe pump set initially at a target concentration of 8 μg ml⁻¹ and then adjusted according to clinical requirements; propofol 2.5–3.5 mg kg⁻¹, thiopentone 4–5 mg kg⁻¹ or 2–3% halothane for induction of anaesthesia followed by 1–2% halothane for maintenance of anaesthesia. All patients breathed a mixture of 70% nitrous oxide in oxygen through a laryngeal mask airway and received an appropriate regional anaesthetic block. Recovery was assessed using the time to achieve full Steward score, open eyes on command, orientation and the time required to complete a simple puzzle. Recovery was slowest with the propofol infusion (mean 39.8 (SD 12.9) min when eyes opened on command). The recovery times were significantly shorter with the three other techniques (propofol bolus 21.9 (9.9) min, thiopentone 23.4 (11.3) min, halothane 20.1 (8.9) min), and the choice among these three methods had no significant influence on the recovery profile. (Br. J. Anaesth. 1994; 72: 554–558)

KEY WORDS

Propofol has been shown to have a superior recovery profile compared with thiopentone for induction of anaesthesia in both adults [1–3] and children [4, 5] undergoing brief surgical procedures. Traditionally, anaesthesia has been maintained in paediatrics with inhalation agents. Recently, having established that propofol infusion is suitable for maintenance of anaesthesia in adults [6, 7], there has been increased interest in using propofol for induction and maintenance of anaesthesia in children [8–13].

The aim of this study was to compare the recovery characteristics of propofol infusion for induction and maintenance of anaesthesia, with three established anaesthetic techniques—propofol, thiopentone or halothane for induction of anaesthesia, followed by halothane for maintenance of anaesthesia—in children undergoing minor surgical procedures.

PATIENTS AND METHODS
We studied 163 healthy Chinese children, aged 3–12 yr, undergoing body surface surgery estimated to take less than 1 h and where a regional anaesthetic block could be performed for analgesia. The study was approved by the Research Ethics Committee of the Chinese University of Hong Kong. Informed consent was obtained from the children's parents. Children were excluded if they were uncooperative, unable to perform a simple child's puzzle, had a history of halothane anaesthesia within the previous 3 months, allergy to any of the study medications or a previous adverse reaction to anaesthesia. Children were allocated randomly to one of four groups: (1) propofol by infusion for induction of anaesthesia, maintenance of anaesthesia with propofol infusion and 70% nitrous oxide in oxygen (group PP); (2) propofol for induction, maintenance of anaesthesia with halothane and 70% nitrous oxide in oxygen (group PH); (3) thiopentone for induction, maintenance with halothane and 70% nitrous oxide in oxygen (group TH); (4) halothane for induction, maintenance with halothane and 70% nitrous oxide in oxygen (group HH). No sedative premedication was given. EMLA cream (lignocaine 25 mg g⁻¹ and prilocaine 25 mg g⁻¹, Astra Pharmaceuticals, Sweden) was applied over the back of both hands approximately 1 h before the time of anaesthesia to assist with i.v. insertion of the cannula.

In group PH and group TH anaesthesia was induced with bolus doses of propofol 2.5 mg kg⁻¹ and thiopentone 4.0 mg kg⁻¹, respectively. Increments were given if necessary up to 1 mg kg⁻¹.
Anaesthesia was maintained with 1–2% halothane and 70% nitrous oxide in oxygen. In group HH, anaesthesia was induced and maintained with 1–3% halothane and 70% nitrous oxide in oxygen. In group PP, anaesthesia was induced and maintained with propofol by continuous i.v. infusion. Patients breathed spontaneously 70% nitrous oxide in oxygen. Propofol was administered by an Ohmeda 9000 syringe pump (Medishield, U.K.) controlled by a 386SX IBM compatible laptop computer via a RS 232C serial interface. The pharmacokinetic model-controlled program was based on our modification [14] of that of Marsh and colleagues [15] for our local paediatric population. The technique is described in detail elsewhere [14]. The target concentration of propofol in blood was set initially at 8 μg ml⁻¹ at induction and the concentration was adjusted subsequently according to standard clinical criteria to maintain an adequate level of anaesthesia. In group PP, the induction dose of propofol was calculated from the theoretical target blood concentration (8 μg ml⁻¹) and our revised central volume of distribution (432 ml kg⁻¹). The mean infusion rate was derived by dividing the total propofol maintenance dose by the duration of anaesthesia.

Lignocaine 2%, at a dose of 0.2 mg kg⁻¹ i.v., was given just before administration of propofol in groups PP and PH to reduce pain on injection. A Rees modification of Ayres T-piece and laryngeal mask airway was used for children who weighed less than 20 kg. The anaesthetic circuit was changed to a Magill system in those above this weight. Quality of induction of anaesthesia was graded as good (induction eventful), adequate (presence of minor side effects which did not interfere with induction) or poor (presence of severe side effects which caused difficult induction).

The depth of anaesthesia in all patients was adjusted according to standard clinical criteria to prevent movement in response to surgical stimuli and to maintain arterial pressure and heart rate within 20% of baseline. Analgesia was provided by an appropriate regional nerve block and rectal paracetamol 0–20 mg kg⁻¹ given immediately after induction of anaesthesia. Arterial oxygen saturation, non-invasive arterial pressure, heart rate and capnograph (HP 78356A, Hewlett Packard, CA, U.S.A.) were monitored throughout the procedure. All anaesthetic agents were discontinued at the same time as closure of the surgical incision. The laryngeal mask was removed at this time.

Recovery was assessed by our recovery room nurses who were unaware of the anaesthetic technique. The following were recorded: (1) time from end of anaesthesia (discontinuation of anaesthetic agents) to achieving a full Steward score [16] (0, 1 or 2 points were given to each of the three categories of conscious level, airway control and movement. The maximum possible score was 6); (2) time from end of anaesthesia to opening eyes and other simple activities on command; and (3) time from end of anaesthesia to orientation to name and age. Psychomotor recovery was assessed by a simple children’s jigsaw puzzle. The puzzle comprised six different shapes and colours which needed to be placed in the appropriate places. All children were trained before anaesthesia by a research nurse who was not involved in the management of anaesthesia. The shortest time of three attempts to complete the task was recorded as the preoperative baseline time. This test was repeated at 30 min and 1 h and 2 h after anaesthesia. All side effects and adverse reactions during the study were recorded. Rescue analgesia consisted of a parenteral opioid prescribed by the anaesthetist.

Statistical analysis

Our sample size for the four groups was calculated assuming a two-sided significance level of 0.05 and a power of 95% to detect differences between groups similar to those reported in three previous studies [8, 9, 13].

Data were analysed with SAS version 6 (SAS Institute Inc, NC, U.S.A.) operated on an IBM computer. Patient and preoperative psychomotor test data were compared using analysis of variance (ANOVA) or chi-square test as appropriate. The postoperative psychomotor test data were analysed using a k-sample Van der Waerden test. In this test the times taken to complete the puzzle were ranked according to their values. Highest possible ranks were given to those patients who could not perform the test because of sedation. The ranks were then transformed into normal scores for the analysis. Significant results from the ANOVA and non-parametric k-sample test were compared further using Dunnett’s t test or two-sample Van der Waerden test with adjustments to the P values where appropriate. The differences between the preoperative and postoperative psychomotor data were compared by Wilcoxon's sign rank test. P < 0.05 was considered statistically significant.

RESULTS

Data from five cases were excluded from analysis because these children required opioid administration to relieve postoperative pain before the end of the study period. Patient data (table I) were similar in the four groups. Anaesthesia details and side effects are listed in table II. Duration of anaesthesia was similar in the four groups. In group PH, the mean induction dose was 2.9 (SD 0.8) mg kg⁻¹. The mean dose of thiopentone in group TH was 4.7 (0.6) mg kg⁻¹. In group PP, the calculated induction dose of propofol was 3.5 mg kg⁻¹ and the mean infusion rate of propofol was 27.3 (8.1) mg kg⁻¹ h⁻¹ (range 7.6–44.5 mg kg⁻¹ h⁻¹). There were no significant differences in the grading of quality of induction of anaesthesia between the groups (P = 0.114). Pain on injection was observed only in groups PP and PH. Apnoea was significantly more frequent in group PP (P = 0.001). The lungs of one child in group PP had to be ventilated by hand throughout the procedure, yet the patient had movement in response to surgical pain on several occasions after attempts to decrease the infusion rate. Breath-holding was observed in one patient in group HH. Involuntary movements were noted in the three groups which received an i.v. anaesthetic agent...
(groups PP, PH and TH) and were more frequent with propofol than with thiopentone ($P = 0.001$). During operation, respiratory complications were observed in group PP whereas arrhythmias were noted in groups TH and HH (table II).

Recovery times for the four groups are shown in table III. After operation, children in group PP were slower to wake up. Times from the end of anaesthesia to achieving all recovery objectives (full Steward score, open eyes on command and orientation in name and age) were significantly longer for group PP compared with those for the other three groups ($P = 0.0001$). Recovery times in groups PH, TH and HH were similar. In group PP, the calculated mean propofol concentration at discontinuation of the infusion and anaesthesia was 4.9 (range 2.5–8.0) $\mu$g
RECOVERY AFTER PROPOFOL INFUSION IN CHILDREN

The aims of this study were to evaluate propofol infusion for induction and maintenance in paediatric anaesthesia and to compare its recovery characteristics with three conventional anaesthetic techniques. Comparability of the depth of anaesthesia with the different anaesthetic techniques may be questioned. There are still many limitations to the objective monitoring of central nervous system sedation, especially in paediatric practice. Hence, in common with other paediatric studies, we have used the standard clinical criteria to match and maintain a comparable level of anaesthesia between the groups.

In group PP, an initial target blood concentration of propofol of 8 μg ml⁻¹ was set for induction of anaesthesia. This was based on the findings from our pilot study of 10 cases [14]. The quality of induction was not different from the three other groups (P = 0.114). However, recovery was significantly slower in group PP compared with the three other groups. The children took twice as long to achieve the recovery objectives (table III). This was both statistically and clinically significant. This finding is in contrast with the other paediatric studies [8, 9, 10, 13]. Puttick and Rosen [8] and Borgeat and colleagues [9] observed a more rapid recovery after propofol anaesthesia compared with thiopentone induction and maintenance with halothane in dental and ENT patients, respectively. Martin, Nicolson and Bargas reported no difference in the recovery time after anaesthesia for total propofol anaesthesia compared with halothane anaesthesia in paediatric outpatients [10]. However, the methodologies in these studies were different from our study. In both the studies by Martin, Nicolson and Bargas [10] and Borgeat and colleagues [9], patients’ lungs were ventilated after neuromuscular block. Puttick and Rosen used intermittent bolus doses of propofol during maintenance of anaesthesia [8] and the duration of the procedures was less than 10 min. Although the anaesthetic technique used for our group PP was remarkably similar to that of the propofol infusion group in the study by Doyle, McFadzean and Morton [13] they observed no difference in the recovery times after anaesthesia using either propofol infusion or propofol bolus followed by maintenance with halothane. In contrast, our propofol infusion group took twice as long as the propofol bolus group to recover.

In the study by Doyle, McFadzean and Morton [13], the initial target blood concentration of propofol set at induction was in the range 8–14 μg ml⁻¹ and our concentration was set at 8 μg ml⁻¹ and then adjusted accordingly. The mean total dose used in their infusion group was 17.9 (range 4.8–28.3) mg kg⁻¹ [N. S. Morton, personal communication] which was similar to the dose in our group PP (17.1 (range 10–31.9) mg kg⁻¹). Their mean target blood concentration at the end of anaesthesia was 5.8 (4–10) μg ml⁻¹ [N. S. Morton, personal communication] which was slightly greater than the concentration of 4.9 (2.5–8) μg ml⁻¹ in the present study. The estimated blood concentration of propofol at the time when their patients woke up was 1.4 (0.3–2.6) μg ml⁻¹. This was again slightly greater than that in our patients (0.97 (0.4–1.9) μg ml⁻¹). Our patients required 39.8 (15–70) min to open eyes on command whereas the children in their study required only 13.5 (4–36) min to wake up and open eyes spontaneously. The pharmacokinetic model developed for our children had a 25% greater volume of distribution than the model developed in Glasgow [14]. This indicates that patients in our study were maintained at lesser plasma concentrations than the patients in the study by Doyle, McFadzean and Morton [13]. Therefore, the difference in recovery was not caused by excessive doses of propofol being given to patients in our study. However, the

ml⁻¹, at the time of opening eyes on command 0.97 (0.4–1.9) μg ml⁻¹ and at the time of orientation 0.9 (0.5–1.5) μg ml⁻¹.

The mean times taken to perform the puzzle before operation were similar for the four groups (P = 0.851). After anaesthesia, there was impairment in psychomotor performance in all four groups and the times taken to complete the puzzle at all times were significantly longer than before operation (P = 0.0001). The performance by group PP was the worst in terms of the number of patients who were able to do the puzzle and the time required to complete the task at 0.5 h (P = 0.0001) and at 1 h after anaesthesia. Group PH scored best, but not significantly better than groups TH and HH. Although the difference between all four groups had disappeared at 2 h, there was still 22–28% impairment in performance compared with baseline (table IV).

The incidence of postoperative side effects is shown in table V. Group PH had the least problems. The incidence of restlessness and disorientation was greatest in group HH with groups PH and TH intermediate. Statistical analysis was not carried out on the incidence of side effects.

DISCUSSION

<table>
<thead>
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<th>TABLE V. Postoperative complications (No. of patients)</th>
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<tr>
<td>Group PP</td>
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<tr>
<td>(n = 38)</td>
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<tr>
<td>Giddiness</td>
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<tr>
<td>Drowsiness</td>
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<td>Restlessness/disorientation</td>
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<td>Cry/uncooperative</td>
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<td>Headache</td>
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<td>Nausea/vomiting</td>
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difference in recovery time cannot be explained fully by the pharmacokinetic differences between the two groups and it is possible that there is an ethnic difference in the pharmacodynamic profile of the drug in the two populations. This suggestion is supported by the longer time required by our patients to recover after induction with propofol and maintenance with halothane (21.9 min) compared with those patients who had a similar anaesthetic in the study by Doyle, McFadzean and Morton (10.5 min) [13].

The three conventional techniques (propofol, thiopentone or halothane induction followed by maintenance with halothane: groups TH, PH and HH) had similar recovery characteristics. Recovery appeared to be more dependent on the maintenance agent rather than the induction agent, as has been observed previously by Runcie and colleagues for anaesthesia lasting longer than 30 min [5].

Psychomotor performance using the time to complete a simple puzzle was included in the assessment to compare recovery of coordination ability. Recovery of psychomotor performance in children who had received the propofol infusion was significantly slower than those who had received propofol, thiopentone or halothane for induction and maintenance with halothane. Psychomotor tests have not been used commonly in paediatric studies. We found the test easy to perform and it discriminates degrees of sedation better than simple tests based on conscious state. Psychomotor recovery appeared comparable with previous adult studies [17], indicating that recovery from anaesthesia is no more rapid in children.

Compared with thiopentone, propofol produced a greater incidence of involuntary movements and respiratory complications at induction. But during maintenance with propofol, there were no arrhythmias and a lesser incidence of emesis at recovery compared with halothane. The side effects observed were not serious.

In summary, propofol for induction and maintenance of anaesthesia was unsatisfactory in our paediatric population. It was associated with delayed early recovery after operation. This result is in contrast with a recent study by Doyle, McFadzean and Morton [13] using a similar technique, but the reasons for the difference are not clear. There were no clinically relevant differences in the quality of the three other techniques for induction and maintenance of anaesthesia and recovery profiles were similar.

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REFERENCES