# Assessment of immediate post-anaesthetic recovery in young children following intravenous morphine infusions, halothane, and isoflurane

Herbert M. Chinyanga M SC MD FRCP(C),
Hilde Vandenberghe PH D,
Stuart MacLeod, MD PH D FRCP(C),
Steven Soldin, PH D, Laszlo Endrenyi PH D

*Within 15 minutes of terminating general anaesthesia, progressive recovery of consciousness, spontaneous ventilation and cough, and limb movements were assessed in 60 young children (age range 0–5 years, mean ± SEM; 2.83 ± 0.34; weight 13.86 ± 0.41 kg). All patients were ASA physical status class I–III, received a standard intravenous induction (atropine 0.02 mg·kg$^{-1}$, thiopental sodium 5 mg·kg$^{-1}$, diazepam 0.2 mg·kg$^{-1}$), were intubated with an orotracheal tube following the administration of metocurine, 0.4 mg·kg$^{-1}$, and were maintained under general anaesthesia with nitrous oxide and oxygen in a 70:30 mixture administered by a T-piece circuit. They were ventilated mechanically to maintain normal blood– oxygen tension and normocarbia.*

*The patients were assessed in three equal groups according to the anaesthetic supplement they received. Group I received intravenous infusions of morphine sulfate (loading dose 60 μg·kg$^{-1}$ administered over 5 minutes followed by a continuous intravenous infusion of 2 μg·kg$^{-1}$·min$^{-1}$. Patients in Groups II and III had 0.5 per cent halothane and 1.0 per cent isoflurane respectively added to the nitrous oxide/oxygen fresh gas mixture rather than morphine sulphate infusions.*

*By the end of the study period, there was no significant difference in the degree of recovery between the morphine and the isoflurane groups but the patients in the halothane group had recovered to a lesser degree. Generally, the patients in the morphine group were awake but not crying, while those in the other two groups were less sedated.*

**Key words**

RECOVERY: postanaesthetic; ANALGESICS: morphine infusion; ANAESTHETICS, VOLATILE: halothane, isoflurane.

One of the most important aims of anaesthesia is to guarantee predictably prompt but quiet emergence from anaesthesia, with recovery of laryngeal reflexes and satisfactory ventilation. The balanced anaesthesia technique (intravenous narcotic in combination with a muscle relaxant, a mixture of nitrous oxide and oxygen, and artificial ventilation) attempts to achieve this objective while simultaneously providing postoperative analgesia and sedation.

In contrast, the use of inhalation agents, halothane in particular, is sometimes complicated by serious laryngospasm at light plains of anaesthesia,

From the Departments of Anaesthesia, Biochemistry, and Clinical Pharmacology, The Hospital for Sick Children and the University of Toronto, Toronto, Ontario.

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*Address correspondence to*: Dr. H.M. Chinyanga, Department of Anaesthesia, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario, M5G 1X8.

which is avoided only by meticulous attention to detail on the part of the anaesthetist.[1]

This paper describes the postanaesthetic recovery in children under five years of age after balanced anaesthesia in which morphine was administered as a bolus injection followed by a continuous intravenous infusion. In two other groups of patients, included in this report for comparative purposes, 0.5 per cent halothane or 1 per cent isoflurane was substituted for the morphine.

## Methods

Sixty patients up to five years old (ASA physical status class I–III), scheduled for various surgical procedures lasting more than 1.5 hours, were selected for this study. The children were free of hepatic and renal diseases, and had no central nervous system disturbances or abnormalities of neuromuscular function.

Routine preoperative history and physical examination as well as appropriate laboratory examinations were performed on each patient. The parents were requested to sign the routine consent forms for the surgical procedure planned as well as a specific consent form approved by the Human Experimentation Committee of The Hospital for Sick Children for the administration of morphine by continuous infusion. The patients to whom morphine was administered constituted Group I, and made up the original experimental series. The patients in Group I, as well as those in the other two groups, received no premedication. Patients in Groups II and III were included in the study at a later stage.

At the time of entering the operating room, a blood pressure cuff, precordial stethoscope, and electrocardiograph electrodes were placed on the patient for monitoring blood pressure and heart rate during induction of anaesthesia and throughout surgery. In all patients, anaesthesia was induced intravenously with a mixture of thiopental sodium, 5 $mg \cdot kg^{-1}$ and atropine, 0.02 $mg \cdot kg^{-1}$, followed by diazepam 0.2 $mg \cdot kg^{-1}$. To facilitate endotracheal intubation, metocurine, 0.4 $mg \cdot kg^{-1}$ was administered intravenously. After the vocal cords were sprayed with lidocaine, 3 $mg \cdot kg^{-1}$, the patients were intubated orally with non-cuffed plastic endotracheal tubes, whose external diameter allowed for a slight gas leak when positive pressure of 2.67 to 4.00 kPa (20 to 30 mmHg) was applied by partially occluding the open end of the reservoir bag of the Jackson-Rees T-piece circuit. Anaesthesia was maintained with a 70:30 mixture of nitrous oxide and oxygen. To maintain normocarbia, the fresh gas flow rate of the anaesthetic gases was adjusted using the formula developed by Rose and Froese.[2] This was confirmed by analysis of arterial blood in patients sampled randomly. In all patients a peripheral vein was cannulated for administration of drugs, fluids, and blood during and after surgery.

Throughout the surgical period, blood pressure, heart rate, body temperature, and blood loss were monitored and appropriate corrective actions taken to maintain normal cardiorespiratory stability. Adequate muscle relaxation was maintained with the aid of a nerve stimulator* and administration of appropriate additional doses of metocurine.

The patients in the experimental group had the radial artery cannulated for intra-operative monitoring of blood pressure and withdrawal of blood samples for analysis of blood gases and serum electrolytes. Serum morphine concentrations were also measured in samples obtained from this site. A second peripheral vein was cannulated for the administration of morphine using a syringe infusion pump.†

Using pharmacokinetic parameters developed by Dahlström *et al.*,[3,4] we tested, modified and subsequently adopted for this study a dosing regimen for morphine that consisted of a loading dose of 60 $\mu g \cdot kg^{-1}$ administered intravenously over five minutes followed by a continuous infusion at a rate of 2 $\mu g \cdot kg^{-1} \cdot min^{-1}$. The infusion rate was double that calculated on the basis of studies of Dahlström *et al.*[3,4]

Since the morphine assay can be done on 100 µL serum, blood samples of volume less than 0.5 ml were withdrawn for determination of morphine serum concentration at 1, 3, 5, 10, 15, 20, 30, 45, 60, 90, 120, 150, and 180 minutes after the loading dose had been administered. In some patients, only two or three blood samples were collected during surgery, and one was drawn at the end of the operation before the morphine infusion was discontinued. Quantitation of morphine in serum or plasma was performed by the technique of high

*Professional Instruments Co., Peripheral Nerve Stimulator NS – 2A Houston, Texas.

†Syringe Infusion Pump Model 2620, Harvard Apparatus, Millis, Mass.

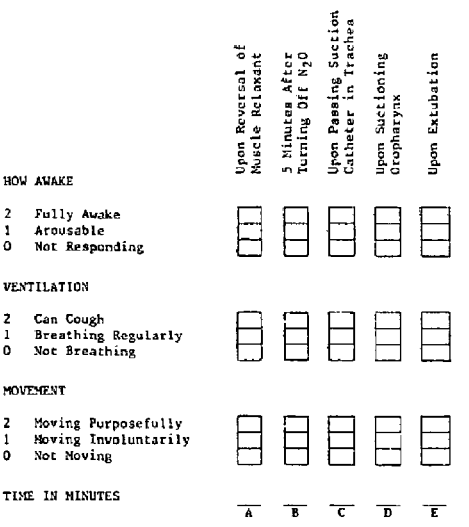


FIGURE 1 Postanaesthetic recovery score chart allows progressive assessment of recovery of consciousness, ventilation, and movement. The highest total score possible at each recovery period is six.

performance liquid chromatography using an amperometric detector.[5]

When surgery was completed and the wound dressing had been applied, while the morphine infusion was still running, the degree of postanaesthetic recovery was assessed using a modification of the recovery room score developed by Steward[6] (Figure 1). The neuromuscular blockage was reversed with neostigmine 0.08 $mg \cdot kg^{-1}$ and atropine 0.04 $mg \cdot kg^{-1}$. Recovery to adequate neuromuscular transmission (sustained tetanus at 50 Hz for five seconds) was assessed using a blockage monitor.

Following the completion of the study with morphine infusion, an identical study was performed in two randomized groups of patients of the same age range. There were 20 patients in each group and halothane 0.5 per cent (Group II) or isoflurane 1.0 per cent (Group III) was administered in the fresh anaesthetic gases. This treatment replaced the previously used morphine infusions. At the completion of surgery the mechanical ventilation continued, but the inhalation anaesthetic (halothane or isoflurane) was turned off for five minutes before the assessment of postanaesthetic recovery began. Except for this, the three groups of patients were treated in identical fashion.

Differences in recovery scores, age, and weight among the three anaesthetic treatments were tested for significance, using one-way analysis of variance and Duncan's Multiple Range Test.

## Results

The means and standard deviations of age, weight, and duration of anaesthesia of all patients in the three groups are shown in Table I. There was no significant difference in the duration of anaesthesia for Groups II and III.

The surgical procedures and number of patients anaesthetized with the three anaesthetics are shown in Table II. Procedures of most surgical specialties were performed including open heart surgery but not neurosurgery.

For the 20 children to whom morphine was administered by infusion, the mean concentration of morphine in the serum at steady state was 55.9 ± 2.43 $\mu g \cdot L^{-1}$ (SEM). The mean serum concentration curve of morphine in the six children over three hours is shown in Figure 2. This provided intraoperative anaesthetic conditions similar to those achieved with 0.5 per cent halothane or 1.0 per cent isoflurane. In order to prevent the appearance of

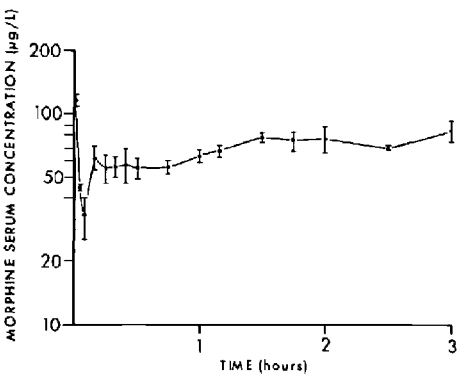


FIGURE 2 Mean serum concentrations of morphine up to three hours after the loading dose of 11 $\mu g \cdot kg^{-1}$ followed by a continuous intravenous infusion at a rate of 2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ morphine sulphate was administered in the first six children studied. Circles represent the mean concentrations and vertical bars the standard error of the mean.

TABLE I Immediate postanaesthetic recovery scores

| *Anaesthetic agent* | *Age (years)* | *Weight (kg)* | *Duration of anaesthesia* | *Recovery stage* | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | *A* | *B* | *C* | *D* | *E* |
| Morphine | | | | | | | | |
| Mean | 3.22 | 14.90 | 3.06 | 0.30 | 2.10 | 5.40 | 5.80* | 5.80 |
| SD | 1.37 | 2.65 | 0.55 | 1.10 | 2.80 | 1.40 | 0.50 | 0.70 |
| Halothane | | | | | | | | |
| Mean | 3.07 | 15.90 | 1.95 | 0.60 | 2.80 | 4.60 | 4.80 | 5.00† |
| SD | 1.51 | 4.22 | 0.20 | 0.90 | 2.00 | 4.40 | 1.30 | 1.30 |
| Isoflurane | | | | | | | | |
| Mean | 2.14 | 11.81 | 2.03 | 0.30 | 2.80 | 4.90 | 5.20 | 5.80 |
| SD | 1.64 | 5.23 | 0.20 | 0.90 | 2.30 | 1.00 | 1.00 | 0.60 |

See text for details of recovery stages.
*At Stage D, the morphine group score was significantly higher than the halothane score ($p < 0.01$).
†At Stage E, the morphine and isoflurane group scores were significantly higher than the halothane score ($p < 0.05$).

TABLE II Surgical procedures performed

| *Procedure* | *Number of patients* | | | |
|---|---|---|---|---|
| | *Group I (Morphine)* | *Group II (Halothane)* | *Group III (Isoflurane)* | *Total* |
| Repair of hypospadias | 4 | 6 | 8 | 18 |
| Orchidopexy | 1 | 10 | | 11 |
| Repair of cleft palate | 2 | | 3 | 5 |
| Ureteral reimplantation | 1 | 1 | 1 | 3 |
| Repair of atrial septal defect | 3 | | | 3 |
| Repair of urethra | 1 | 1 | | 2 |
| Repair of outstanding ears | | | 2 | 2 |
| Repair of hydrocele | 1 | | | 1 |
| Repair of fistula of palate | 1 | | | 1 |
| Resection of vascular ring | 1 | | | 1 |
| Excision of pre-auricular tags | | | 1 | 1 |
| Pyeloplasty | | | 1 | 1 |
| Excision of lymphangioma of foot | | 1 | | 1 |
| Resection of cystic hygroma | 1 | | | 1 |
| Excision of giant hair nevus of temple | | 1 | | 1 |
| Lower lobectomy | 1 | | | 1 |
| Closure of cutaneous pyelostomy transurethral resection of urethral valves | | | 1 | 1 |
| Soeve pull through | | | 1 | 1 |
| Ligation of patent ductus arteriosus | 1 | | | 1 |
| Cystoscopy | | | 1 | 1 |
| Excision of thyroglossal duct cyst | | | 1 | 1 |
| Repair of microtia | 1 | | | 1 |
| Resection of coarctation of the aorta | 1 | | | 1 |
| Total | 20 | 20 | 20 | 60 |

clinical signs of inadequate anaesthesia, the morphine infusion had to be initiated at least 15 minutes before the surgery began.

In the morphine and isoflurane groups, when the first surgical stimulus (towel clips or incision) was applied within ten minutes of beginning the administration, there was a transient rise in both heart rate and blood pressure. In the morphine group this rise corresponded to the distribution phase after the morphine loading dose.

Patients whose serum morphine concentration was in excess of $80\,\mu g \cdot L^{-1}$ at recovery showed clinical signs of narcotic overdose of varying degrees. This was reversed with naloxone hydrochloride (Narcan) $1.5–3.0\,\mu g \cdot kg^{-1}$ administered intravenously.

At stage A (reversal of muscle relaxant) recovery of spontaneous ventilation occurred in some patients who had received halothane or isoflurane (Table I). The patients in the morphine group remained apnoeic. Overall at stage A, the difference in recovery was not statistically significant.

At stage B (5 minutes after $N_2O$ was turned off) a few patients in the morphine group opened their eyes spontaneously late in the assessment period. Again, the differences in recovery time among the three groups were not significant.

When the patients were stimulated by passing a suction catheter tip into the trachea through the endotracheal tube (recovery stage C), the degree of recovery in the three groups did not differ significantly.

After the oropharynx was stimulated by suctioning with a metal suction tip (recovery stage D), the degree of recovery of the morphine group was significantly better than in the halothane group but was not different from that of the isoflurane group.

After the patients were extubated (Stage E), the halothane group scored significantly lower than the other two groups. There was no significant difference between the morphine and the isoflurane groups at this interval.

None of the groups subsequently deteriorated in their degree of recovery on admission or during their stay in the recovery room. In most cases, unlike patients in the halothane or isoflurane groups who needed administration of postoperative analgesic drugs, the patients in the morphine group were well sedated, breathing easily and regularly, and, at least in the four- to five-year-old age range, rational in their response when aroused and spoken to. The recovery scores of the morphine group were better, although the duration of surgery and anaesthesia had been considerably longer ($3.06 \pm 0.55$ hours compared with $1.95 \pm 0.20$ and $2.03 \pm 0.20$ hours respectively).

## Discussion

A general anaesthetic is usually considered satisfactory when it prevents pain and unpleasant memories of surgical events, maintains or improves the function of vital systems, and guarantees a predictable, prompt, but quiet, and uncomplicated recovery.

Halothane, still the most popular anaesthetic in children, presents some intraoperative and postoperative problems, namely hypotension, bradyarrhythmias, and postextubation laryngospasm.[1] However, in our series of 20 children, there was only one case of vomiting after extubation. Although the patients were drowsy, as indicated by their relatively low postextubation scores, they presented no respiratory or ventilatory problems during their stay in the recovery room.

Isoflurane is a new inhalation anaesthetic that has not yet been used extensively in children.[7,8] Already, however, it appears to offer several advantages over halothane in paediatric patients.[9] Because of its low solubility coefficient, it has a rapid onset of action. It is eliminated with little metabolism. This ensures a faster recovery from the anaesthetic state than with an equivalent concentration of halothane. With isoflurane there appears to be less myocardial depression and a more stable heart rhythm.

In our series, although the isoflurane group scored better than the halothane group in recovery Stages C through E, the only statistically significant difference in the scores was in Stage E, after extubation. Although these two groups were randomized, in the final analysis it was noted that the isoflurane patients were significantly younger and smaller than the other two groups. The effect of this finding on the degree of recovery compared to the halothane group cannot be discounted. However, when either of these two inhalation anaesthetics is used, the patient needs immediate postoperative analgesia to ensure sedation.

The use of narcotics, particularly morphine, in children has also been associated with problems,

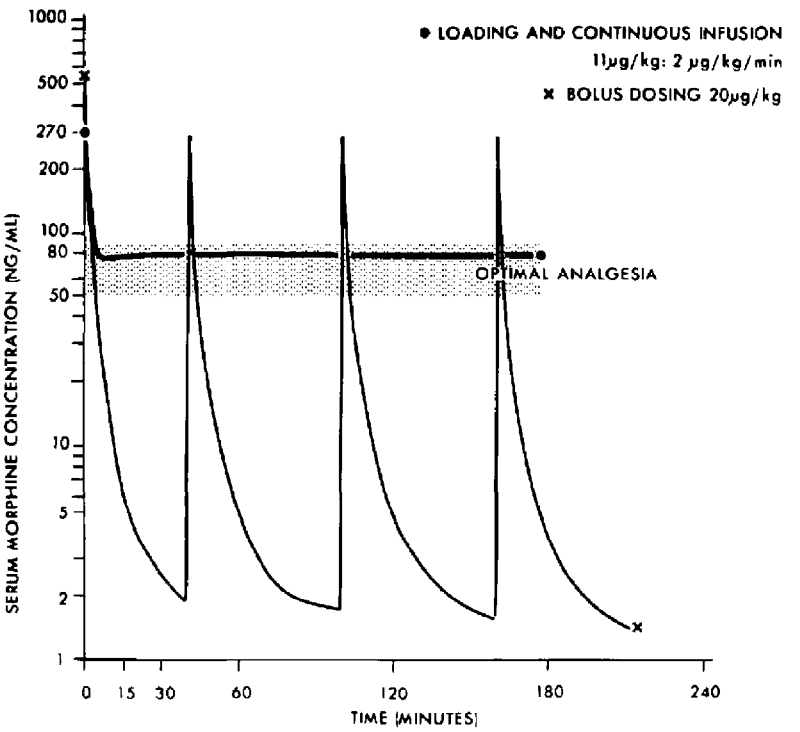


FIGURE 3 Simulated curves comparing serum morphine concentrations administered by two techniques, (A) —●— loading dose 11 $\mu g \cdot kg^{-1}$ followed by continuous infusion at 2 $\mu g \cdot kg^{-1} \cdot min^{-1}$, (B) —×— a 20 $\mu g \cdot kg^{-1}$ bolus every 60 minutes. The shaded strip indicates the range of serum morphine levels (52 to 82 $ng \cdot ml^{-1}$) associated with optimal intraoperative analgesia.

the most important of which is overdose resulting in serious respiratory depression. More importantly, infants appear to be more sensitive to the central nervous system depressant effects of narcotics than do older children.[10,11] On the other hand, clinical signs of pain during surgery have been reported in children aged one to seven years when the mean morphine serum concentration falls below 65 $\mu g \cdot L^{-1}$ (95 per cent confidence limits = 46–83 $\mu g \cdot L^{-1}$).[4]

Because of lack of precise clinical indices reflecting additional dosage needs, it is difficult to administer an optimal amount of narcotic in young children within the age range of the present study, using a bolus technique. Heart rate, blood pressure, and sweating, parameters indicating surgical stress, are very poor guides.[12] Young children often do not diaphorese and may manifest a high heart rate and blood pressure in the face of what should be a sufficient narcotic dosage.

The standard technique of administering narcotics in bolus form produces periods in which the narcotic level may be sub-analgesic (Figure 3). The most rational approach, therefore, is to give a loading dose followed by a continuous intravenous infusion to maintain the serum concentration within the analgesic range.[13,14] In our series, a mean level of 55.9 ± 2.43 $\mu g \cdot L^{-1}$ (mean ± SEM), well within the findings of Dahlström *et al.*,[3,4] provided satisfactory intraoperative anaesthetic conditions with good recovery of laryngeal reflexes, ventilation, awareness, and limb movement.[4] Serum concentrations below that were associated with clinical signs of inadequate anaesthesia.

It is necessary to keep the patient well relaxed with adequate doses of muscle relaxants in order to reduce sensory impulse traffic from skeletal muscles as this reduces anaesthetic requirement.[15,16] This is a light form of anaesthesia. Its aim is to have the pain component of the surgical manipulations suppressed continually by adequate narcotic analgesic. The other sensory impulses (e.g., pressure, muscle and joint sense) are suppressed by the combined effect of the sedative properties of the narcotic, nitrous oxide and diazepam.[17–19] These drugs lower MAC in man.[16–19]

Broadly, the intraoperative anaesthetic conditions in the morphine group, as assessed by heart rate and blood pressure changes, were similar to the halothane and the isoflurane group. The morphine group tended to exhibit consistently higher blood pressure measurements. After the recovery period, most of the patients in the morphine group were free of pain and better sedated for one to two hours without needing additional postoperative analgesia. They experienced no respiratory difficulty, and had an uneventful stay in the recovery room. The older children in our series stated that they had not been aware of the surgical procedure.

Therefore, we believe that morphine administered by this technique can be a valuable tool in providing safe anaesthesia for major surgery in young children. Used with the continuous infusion technique described, it should also result in a prompt but quiet recovery free of the complications sometimes associated with inhalation anaesthetics. Other, newer, narcotics with special pharmacological properties, if administered in the same rational fashion, will probably achieve similar results.

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## Résumé

*Cette étude a porté sur 60 jeunes enfants, de 0 à 5 ans et pesant en moyenne 13.8 kilos.*

*A moins de quinze minutes, à la suite d'anesthésies générales, nous avons évalué le retour progressif de la conscience et de la ventilation spontanée et avons noté la présence des mouvements des membres. Tous les enfants étaient de classe 1–3 A.S.A. et avaient reçu une induction intraveineuse normalisée constituée d'atropine à 0.02 mg·kg$^{-1}$ de thiopenthal sodique à 5 mg·kg$^{-1}$ et de diazépam à 0.2 mg·kg$^{-1}$. Tous ont été intubés par voie oro-trachéale et l'anesthésie entretenue avec du protoxyde d'azote et de l'oxygène dont un mélange à 70/30 administré par un système avec pièces en T. Ils étaient ventilés mécaniquement pour maintenir les tensions d'oxygène et de $CO_2$ à l'intérieur de la normale.*

*Les malades ont été répartis en trois groupes (20 malades par groupe) selon la médication anesthésique adjuvante qu'ils ont reçue. Le groupe I a reçu des infusions intraveineuses de morphine. La dose d'amorce était de 60 μg·kg$^{-1}$ injectée sur une période de cinq minutes. Cette dose était suivie par l'infusion continue de 2 μg·kg$^{-1}$ par minute. Pour les malades du groupe II et III de l'halothane à 0.5 pour cent et de l'isoflurane à un pour cent respectivement ont été rajoutés au mélange des gaz frais.*

*A la fin de la période d'observation, les malades du groupe halothane étaient moins alertes que ceux des deux autres groupes. Il n'y avait pas de différence significative dans le degré d'éveil entre les malades du groupe morphine et isoflurane. En général, les malades du groupe morphine étaient éveillés mais ne pleuraient pas, alors que ceux des deux autres groupes apparaissaient moins calmes.*