Recovery after anaesthesia with alfentanil or halothane

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Seventy-three patients were studied during and after anaesthesia with either alfentanil or halothane for surgical procedures of short duration. The procedures were minor gynaecological or minor urological procedures, involving males and females between the ages of 21 and 86 years. After pre-medication with lorazepam, anaesthesia was induced with methohexitone and continued with nitrous oxide and oxygen, supplemented with halothane (34 patients) or alfentanil (39 patients). Anaesthesia was generally smooth and uncomplicated except that at induction 22 of the patients receiving alfentanil became apnoeic for longer than 30 seconds. Spontaneous respiration resumed without the need for naloxone in any patients. After surgery, recovery of consciousness was significantly more rapid after alfentanil than after halothane (5.6 minutes versus 10.1 minutes). This study demonstrates that alfentanil can be a suitable alternative to conventional general anaesthesia for short cases and may have a useful place when rapid recovery and turnover of cases is important.

Alfentanil is a recently introduced synthetic opioid, chemically related to fentanyl but with a more rapid onset and shorter duration of action.^{1,2} Recovery from anaesthesia with alfentanil may be expected to be very rapid, thus making it a suitable agent for use in day-case surgery and short procedures. This study compares recovery from anaesthesia after alfentanil or halothane.

Key words

ANALGESICS, NARCOTIC: alfentanil; ANAESTHETICS, VOLATILE: halothane; RECOVERY.

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Methods

Seventy-three patients between the ages of 21 and 86 years, who were to undergo elective surgery of short duration, gave informed consent to take part in the study. All patients were to be anaesthetised for short minor procedures; either minor gynaecological surgery involving cervical dilatation, or cystoscopy and allied minor urological procedures. Patients undergoing termination of pregnancy were excluded as the use of halothane was considered inappropriate for this procedure. The trial protocol was approved by the Committee on Safety of Medicines and by the local ethical committee. All the anaesthetics were administered personally by the author.

All patients entering the study received pre-medication approximately 1.5 hours prior to surgery with oral lorazepam 2 mg, and on arrival in the anaesthetic room were randomly allocated to receive either alfentanil (Group A) or halothane (Group B). A small indwelling needle was introduced into a vein on the dorsum of the hand, and anaesthesia induced with methohexitone $1.5 \text{ mg} \cdot \text{kg}^{-1}$ in both groups, preceded in Group A by 500 μg of alfentanil intravenously. Spontaneous complaint of pain or discomfort on injection was recorded, as was the occurrence of hiccoughs. Both groups then received nitrous oxide and oxygen (66 per cent nitrous oxide, 33 per cent oxygen) by face mask. Patients in Group A received supplements of alfentanil and methohexitone as decided by the clinical judgement of the anaesthetist: direct response by the patient to surgical stimulus was treated with alfentanil; other responses were treated with methohexitone. In Group B halothane was added to the inspired gases according to usual practice. Halothane was administered for a mean of 10.3 minutes and at a mean concentration of 1.8 per cent and was not discontinued in anticipation of the

end of surgery. The ECG (CM₅) was continuously monitored in each patient and the patients were closely observed by the anaesthetist for evidence of respiratory depression. If apnoea developed (defined as cessation of respiration for thirty seconds or more), the patient was ventilated by hand until spontaneous respiration resumed. At the end of surgery nitrous oxide (and halothane, if applicable) was withdrawn. The times of all drug administrations were noted, as was the time at which nitrous oxide was discontinued. The patient was taken to the recovery area where the nursing staff were not aware of the group to which the patient belonged.

The assessment of recovery was based on simple observation of waking; every 15 seconds the recovery room staff asked the patient to give their name and to open their eyes. The time at which they were capable of doing so was noted.

Patients were visited 2–3 hours after the end of anaesthesia and questioned about awareness and the acceptability of their anaesthetic. They were also questioned about nausea and vomiting. In addition the nursing staff were asked to report any problems. When possible the patients were seen again the next day and questioned again.

Statistical analysis of results was by the Student's *t*-test, but recovery times followed a skewed distribution and logarithmic transformation was used to obtain mean values. The significance of the difference in recovery times was tested using the Mann-Whitney "U" test.

Results

The patients in each group showed no significant difference in age, weight or sex distribution (Table I). The induction dose of methohexitone and the duration of anaesthesia, measured from the time of the first intravenous injection to the time at which nitrous oxide was discontinued, were also com-

TABLE II Results (Mean $\pm$ S.E.M.)

	Group A	Group B	P
Methohexitone initial dose (mg)	84.4 $\pm$ 2.9	90.9 $\pm$ 2.5	n.s.
Duration of anaesthesia (min)	11.5 $\pm$ 1.2	11.7 $\pm$ 1.2	n.s.
Recovery time (min)	5.6 $\pm$ 1.1	10.1 $\pm$ 1.1	<0.01

parable between the two groups (*t* test, $p > 0.1$) (Table II). Induction of anaesthesia with methohexitone was slightly smoother when preceded by alfentanil, in that hiccoughs were less common and less troublesome in Group A; the incidence of pain on injection was unaffected. Hiccoughs occurred at induction in five patients in Group A and in eight in Group B ($\chi^2 = 0.713$, $0.1 < p < 0.5$). Pain on injection was complained of by six patients, three in each group.

After the initial dose of alfentanil of 500 μ g intravenously, a further increment (200 μ g) was needed in 24 patients at a mean time of 6.9 minutes (range 3–11). Fifteen patients received no extra alfentanil, but nine of these received extra methohexitone. After the first increment (24 patients), further alfentanil was required after a mean interval of four and a half minutes (14 patients). The mean time to additional methohexitone was also four and a half minutes.

In both groups the recovery times were markedly skewed, and logarithmic transformation has been used to obtain the mean value. The mean recovery time after alfentanil was 5.6 minutes (95 per cent confidence limits 3.3–7.9), whilst after an anaesthetic of similar duration with halothane the recovery time was 10.1 minutes (95 per cent limits 7.9–12.4). This difference is statistically significant (Mann-Whitney U test, $p < 0.01$) (Table II).

The chief problem occurring during this study was apnoea. Twenty-two of the thirty-nine patients anaesthetised with alfentanil developed apnoea, whilst only one patient in the halothane group became apnoeic. This difference in incidence is highly significant ($\chi^2 = 21.65$, $p < 0.001$). There was no difference in the incidence of apnoea between the sexes, nor was there any significant change with age.

Sixteen patients became apnoeic at induction, and four patients developed apnoea again when incremental alfentanil was given. Naloxone was not

TABLE I Patient details (Mean $\pm$ S.E.M.)

	Group A (alfentanil)	Group B (halothane)
N	39	34
Male	16	9
Female	23	25
Weight (kg)	63.9 $\pm$ 1.8	64.8 $\pm$ 1.6
Age (yrs)	50.5 $\pm$ 3.5 (Range 21–86)	55.2 $\pm$ 1.1 (Range 34–79)

used at all during this series, and there were no other complications of note.

Recovery was in almost all cases deemed by the recovery ward staff to be satisfactory. Three patients in the alfentanil group were restless on recovery, and one patient vomited. Four patients in the halothane group had a short-lived bout of shivering during recovery.

All patients in the halothane group were prepared to have the same anaesthetic again, but two of the patients who received alfentanil felt so nauseated that they would not wish to receive the drug again. No patient reported awareness during the procedure.

Discussion

Animal studies¹ have shown alfentanil to have extremely rapid onset of action, and Bower and Hull² predicted that the same would be true for man. The rapid onset was especially well seen when an increment was needed to suppress a response to a surgical stimulus, an effect usually being evident in less than one minute. After some practice it was found best to anticipate the need for further analgesia to provide the best possible conditions and further experience with the drug has confirmed its predictability. After the induction dose a mean time of 6.9 minutes elapsed before an increment was required, after which further increments were needed at regular intervals, with no apparent tendency to cumulation. This appears to bear out the observation that the pharmacokinetics of alfentanil carry the possibility of flexible efficient use in anaesthesia.³ Alfentanil's predictability allows relatively easy anticipation of further dosage needs, and helps in the provision of smooth anaesthesia. Initially, whilst learning to use the drug, the technique is not as smooth as inhalation anaesthesia, but with practice it is possible to provide good conditions with the added benefit of flexibility and rapid recovery. It should be noted that 42 per cent of patients required no incremental alfentanil, as judged clinically, and that there is wide variation in pharmacodynamic effect of the drug.³

Age also influences both kinetics and dynamics of alfentanil, and it has been suggested that over the age of sixty-five years the dosage should be reduced.⁴ There was no significant difference in this study between the ages of the patients receiving or not receiving increments of alfentanil, but until

further evidence is available it would seem prudent to use lower doses in the elderly, or at least to expect a longer action from a given dose, as for most drugs.⁵

The major difficulty encountered was a high incidence (50 per cent) of respiratory depression leading to apnoea at induction. This high incidence was disturbing, but continued experience has resulted in a lower incidence of apnoea. Reducing the speed of administration and limiting the induction dose to $5 \mu\text{g}\cdot\text{kg}^{-1}$, when spontaneous respiration is desired, have lessened the frequency of this complication. Kay and Pleuvry⁶ showed that $6 \mu\text{g}\cdot\text{kg}^{-1}$ causes rapid and significant respiratory depression lasting for ten minutes, and 0.5 mg given intravenously to surgical patients had the same effect for 4–5 minutes.⁷ In this latter study 0.5 mg was also found to cause apnoea in five out of 22 patients. Other authors have experienced similarly high rates,^{7,8} whilst others have found lower rates.^{9,10}

It became clear that the rapid administration of alfentanil is a major factor in the development of apnoea. The volume in which the drug is presented ($500 \mu\text{g}$ in 1 ml) renders it difficult to administer over the recommended minimum of thirty seconds and dilution to a concentration of $100 \mu\text{g}\cdot\text{ml}^{-1}$ is helpful in this respect. Thus by a combination of reduced dosage and slower administration apnoea can be much reduced.

Recovery in almost all cases in the alfentanil series was smooth, as was recovery from halothane. Immediate recovery from alfentanil was attained at a mean time of five minutes and the mean recovery time for the halothane group was 12 minutes, significantly longer ($p < 0.01$). Formal psychomotor testing of recovery was not carried out, as this would have been impracticable in the circumstances.

Tests of recovery from anaesthesia are legion, and vary from the simple return of consciousness (as in this study) to the complex psychomotor testing employed by others.^{6,11,12} In this study the ability to respond to simple command was used as the measure of recovery. This ability, together with the ability to answer a simple question, implies the return of consciousness and as such is a reasonable test of immediate recovery from anaesthesia. It is also an end-point which is easy to define, repeatable, has the advantage of requiring no equipment, and does not need trained observers. Inevitably it

does not reflect the speed or quality of return to full normality. However, this study was specifically concerned with immediate recovery, as this aspect has a bearing on the throughput of an operating list, particularly where recovery facilities are limited. On this basis it seems that intravenous anaesthesia has the advantage over inhalational anaesthesia with patients able to return to their ward several minutes earlier. This is in agreement with the work of others¹³⁻¹⁵ using similar techniques, who found recovery times between 3.8 and 6.4 minutes. However, Cooper⁶ reported much shorter recovery times in unpremedicated patients. In this study a benzodiazepine was used as premedication in both groups, which might be expected to exert a hang-over effect.^{16,17} Thus recovery might reasonably be expected to be slightly prolonged, compared to other reports.

The ward nursing staff did not report an increased incidence of nausea and vomiting, which seemed to be no more common following alfentanil than after anaesthesia with other opiates; this is the experience of others when using alfentanil.¹⁸⁻²⁰ It has even been suggested that alfentanil may have an anti-emetic effect,¹ but this was not particularly evident in this study. Indeed it seems unlikely that an opioid drug would have such a property, as this would represent a complete departure from the pharmacology of the group.

Complications with alfentanil were few in this trial, and cardiovascular stability was good. There was no evidence of chest wall rigidity and overall alfentanil performed as predicted for a short-acting opioid, providing stable and satisfactory operating conditions generally acceptable to patients, surgeons and anaesthetists alike.

Whether alfentanil has any advantages over the currently available opioids is open to question; most would predict, on the basis of the kinetics of the drug, a more rapid onset and recovery. Some have found no marked advantage of alfentanil over fentanyl,²⁰ whilst others disagree.¹⁴ This present study cannot address this question, but has shown alfentanil to be a useful alternative to an inhalational agent for anaesthesia for cases of short duration where a rapid recovery and rapid turnover of cases is required. This supports the conclusion of others^{6,21} that it may have a place in outpatient and day-case surgery.

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Résumé

Soixante-treize patients ont été étudiés durant et après anesthésie avec soit l'alfentanil, soit l'halothane pour les procédures chirurgicales de courte durée. Les procédures étaient soit gynécologiques mineures, soit urologiques mineures portant sur des hommes ou des femmes âgés de 21 à 86 ans. Après prémédication avec lorazepam, l'anesthésie a été induite avec le méthohexitone et maintenue avec le protoxyde d'azote et oxygène additionné d'halothane (34 patients) ou d'alfentanil (39 patients). L'anesthésie a été généralement douce, non compliquée à l'exception de l'induction où chez 22 patients recevant de l'alfentanil, on a observé une apnée pour une durée supérieure à 30 secondes. La respiration spontanée a repris sans administration de naloxone pour aucun des patients. Après la chirurgie, le réveil était significativement plus rapide pour le groupe alfentanil que pour celui de l'halothane (5.6 minutes vs. 10.1 minutes). Cette étude démontre que l'alfentanil peut constituer une alternative convenable à l'anesthésie générale conventionnelle pour des procédures chirurgicales de courte durée et peut avoir une place utile quand un réveil rapide est souhaité dans les centres où le débit des cas est important.