

A comparison of the efficacy of Alfentanil and Remifentanil analgesic infusions for spinal surgery

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Summary

The use of alfentanil infusion was compared with that of remifentanil infusion for spinal cord surgery in a retrospective review. The aim was to compare the outcome when methohexitone was used as the only hypnotic agent in the two groups. Over a 3-year period, 5 patients (group 1) had Alfentanil infusion and 11 patients (group 2) had remifentanil infusion for analgesia during spinal cord surgery.

Results showed that remifentanil lead to a faster onset of recovery than alfentanil. It also provided better haemodynamic stability than alfentanil without excessive hypotension ($p > 0.05$). Our experience here indicated that remifentanil provided better flexibility of use with less tachycardia and respiratory depression than alfentanil for spinal surgery.

Keywords: Total Intravenous Anaesthesia, Spinal surgery.

On avait comparé l'usage de l'infusion alfentanile par rapport à l'infusion remifentanile à l'égard de la chirurgie de la moelle épinière à travers un examen rétrospective. Le but était de comparer le résultat quand on a utilisé la méthohexitone comme le seul agent hypnotique dans les deux groupe. Au cours d'une période de 3 ans, 5 malades (groupe 1) avaient l'infusion alfentanile et 11 malades (groupe 2) avaient l'infusion remifentanile pour l'analgésie durant l'opération de la moelle épinière.

Des études montrent que l'efficacité de la remifentanile menant à la guérison est reconnue plus que l'effet d'alfentanile. Egalement, elle assure mieux la stabilité hémodynamique plus que l'alfentanile sans l'hypertension excessive ($P > 0,05$).

D'après notre expérience, on peut conclure que la remifentanile assure mieux la souplesse de la dose avec la diminution dans la tachycardiaque et la crise dans l'appareil respiratoire plus que l'alfentanile à l'égard de l'opération vertébrale.

Introduction

Opioid drugs are sometimes used as part of an induction sequence to provide a smooth onset of anaesthesia and to obtund the haemodynamic responses to laryngoscopy and intubation. Opioids and hypnotic agents can be used together in a Total intravenous anaesthetic regime, the drugs interacting to potentiate one another. The use of a methohexitone-based TIVA regime during spinal column surgery had been reported earlier to provide the greatest potential for non-invasive monitoring of spinal motor tract integrity¹.

Alfentanil was the opioid being used in this centre in combination with various hypnotics such as etomidate. Ketamine and propofol. Methohexitone and alfentanil provided a TIVA based regime that allowed for intraoperative spinal cord monitoring and good wake up times. However, the anaesthetic was associated with a great degree of intraoperative haemodynamic instability. Remifentanil, a new opioid with a pharmacodynamic profile which promises greater flexibility in usage was introduced to correct this. Maintenance of haemodynamic instability in spinal cord surgery is important in order not to jeopardise spinal cord perfusion.

Alfentanil is a synthetic opioid tetrazole derivative of fentanyl, about one-fourth as potent and less lipid soluble, than fenta-

nyl, with a small volume of distribution ($V_d = 0.1-1.01$ per kg) and a higher percentage of protein binding (89-92%)⁴. One of the clinical applications of alfentanil is by continuous infusion. It has a rapid onset of action, short elimination half-life and provides a prompt recovery with temporary residual analgesia. Side-effects include respiratory depression, constriction of the pupils, depression of the cough reflex and suppression of excitatory activity and nausea and vomiting by stimulating the chemoreceptor trigger zone for emesis in the medulla⁴.

Remifentanil is a new congener of the fentanyl family of opioids that was approved for use as a supplement to general anaesthesia in the USA in 1996⁶. Pharmacodynamically, in most regards, remifentanil is indistinguishable from the other fentanyl congeners, producing analgesia respiratory depression and other effects that are typical of the fentanyl relatives. It is unique because of its short-acting profile. Its ester structure renders it susceptible to widespread ester hydrolysis, resulting in very rapid metabolism. It thus constitutes the first true 'ultrashort-acting' opioid. Its elimination and context-sensitive half-time ($t_{1/2}$ context) are significantly shorter compared with alfentanil⁵. Because of the shorter and more predictable recovery profile from anaesthetic effects, we have studied any possible difference in the intraoperative haemodynamic and post operative recovery of spinal surgical patients after total IV anaesthesia (TIVA) with alfentanil-methohexitone or remifentanil-methohexitone.

This is a retrospective study comparing the outcome of the two drugs using times to awakening and tracheal extubation as pharmacodynamic end points.

Patients and methods

The anaesthetic notes of patients who had spinal surgery over a three year period were reviewed. All such patients had a special anaesthetic technique which allowed for intra operative spinal cord monitoring using the transcranial magnetic motor evoked potential (TcMMEP). Twenty one patients were identified. Ten of these patients were given alfentanil infusion while eleven had remifentanil infusion. However, five patients of the alfentanil group also had ketamine administered. These five were excluded to reduce the confounding effect of the hemodynamic effects of ketamine. All patients had methohexitone as the hypnotic agent.

In the alfentanil group, (group 1), three of the patients had thoracolumbar spine surgery while two patients had cervical spine surgery. In the remifentanil group (group 2), nine patients had thoracolumbar spine surgery while two had cervical spine surgery. Neurologically, no patient had a complete spinal cord lesion. They were either neurologically incomplete lesions or they had no neurological deficit.

The anaesthetic technique was standardized. Patients were premedicated with either promethazine or morphine deliberately avoiding benzodiazepines. On patients arrival in the induction room, vital signs were usually recorded using the Hewlett Packard 78 352A cardiac monitor. This recorded the pulse rate, arterial oxygen saturation electrocardiogram, the fractional inspired oxygen ($F_{I_{O_2}}$), end-tidal CO_2 , the percentage inhaled volatile agent and blood pressure. A radial artery cannular was inserted in all cases for invasive blood pressure reading. Anaesthesia was induced with methohexitone 2mg/kg/min for hypnosis. This was followed

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by 100mg/kg/min for 30 minutes. Depending on the cardiovascular response, the dose was decreased to 75-50mcg/kg/min. In group 1, analgesia was provided by a bolus dose of alfentanil 50mcg/kg/min followed by 5mcg/kg/min for 15 min and 1 mcg/kg/min thereafter. In group 2 analgesia was provided by a bolus dose of remifentanil 1 mcg/kg followed by an infusion of 0.5mcg/kg/min. The drugs were administered using computer controlled infusion pumps that rapidly attained, and then maintained, constant drug blood concentrations. If the patient showed signs of inadequate anaesthesia (autonomic or somatic response) target concentration would also easily be increased using the infusion pump. Volatile agents were not used during the anaesthetic. The concentration of nitrous oxide used was such that permitted transcranial magnetic motor evoked potentials (TcMMEP) monitoring, usually less than 25%. The TcMMEP monitor was applied after induction of anaesthesia in all cases.

A neuromuscular blocking agent was used in most instances at induction of anaesthesia for initial airway control but before recording the TcMMEP. In patients having surgery of the lumbar spine, relaxants were also used during patient positioning, muscle stripping or when diathermy was used continuously, to prevent muscle contractions during these periods. Ventilation was controlled initially until recovery of neuromuscular function. Subsequent recovery of neuromuscular function was confirmed by using a conveniently located peripheral motor nerve with a nerve stimulator. The adequacy of the TIVA-based anaesthesia was assessed in relation to cardiovascular stability with the aid of invasive arterial pressure monitoring and the absence of reflex body movements in response to surgical stimuli. Signs of cardiovascular instability were defined as a mean arterial pressure (MAP) above 100mmHg or heart rates above 90 beats per minute in the absence of hypovolemia and autonomic signs such as sweating flushing and somatic responses such as swallowing, movement or coughing.

Approximately ten minutes before the end of surgery in each group, methohexitone infusion was discontinued. In group 1, alfentanil was also discontinued at the same time. In group 2, remifentanil infusion was discontinued just before turning the patient supine. The neurologically intact patients on remifentanil were given intravenous morphine 2.5mg before discontinuing the remifentanil infusion. This was subsequently repeated at 5min intervals as appropriate to a maximum of 10mg.

All patients who were neurologically intact and hence could use the patient-controlled analgesia pump (PCA), had PCA morphine for post-operative analgesia. Others had intravenous morphine infusions. All the patients were given 100% oxygen following termination of infusion in theatre. They were then observed during recovery in order to judge the appropriate time for tracheal extubation, depending on adequacy of respiration (a ventilatory frequency of greater than 10 per min) and conscious level. An allowance was made for a drop in blood levels of infused agents to occur and for signs of recovery of conscious level before doxapram was given if respiration remained markedly depressed. Naloxone was only used if respiration remained markedly depressed despite doxapram. The time to tracheal extubation from cessation of infusion and transfer to post anaesthetic care unit was also noted. Doxapram or naloxone was administered to aid resumption of spontaneous respiration in some instances.

On arrival in the PACU, all patients were observed for at least one hour. The ventilatory frequency, oxygen saturation, pain and level of sedation were routinely monitored. All patients received 40% oxygen by face mask. Pain on movement was assessed using a four point scale of no pain, mild, moderate and severe pain. Patients were discharged to the Spinal Intensive Care Unit or high dependency unit following adequate recovery.

Results were expressed as mean values \pm SD.

Appropriate statistical tests (t-test and percentages) were used

to compare the time to tracheal extubation and the haemodynamic responses in the two groups. The limits of significance were set at $P < 0.05$.

Results

Five patients had alfentanil (Group 1) as the intraoperative analgesic while eleven were given only remifentanil (Group 2). Group 1 patients were relatively younger but not to statistical significance. The groups had a similar weight distribution (Table 1)

Table 1 Demographic data

	Group 1 (n=5)	Group 2 (n=11)
Age (yrs)	37 \pm 18.6(19-54)	38 \pm 20.9(19-82)
Sex	2.3	10.1
Weight(kg)	63 \pm 8.4	68.3 \pm 7.1

Note: Values are mean \pm SD or () range

There were no statistically significant differences

Though the duration of anaesthesia for each group was similar. Group 1 patients required a higher dose of methohexitone to keep asleep. (Table 2) Group 2 patients took a longer time to wake up despite the lower dose of methohexitone. This was not found to be statistically significant.

Table 2 Duration of Anaesthesia and total drug dose

	Group 1	Group 2
Duration of anaesthesia (min)	209(140-290)	215(130-345)
Methohexitone administration (mcg/kg/min)	5.62(0.79)	6.15(2.66)
Alfentanil administration (mcg/kg/min)	0.11(0.04)	-
Remifentanil administration (Mcg/kg/min)	-	0.08(0.04)

Note: values are mean plus standard deviation or () range.

The mean duration to tracheal extubation as shown in Table 3 was 22 \pm 7.2 minutes in Groups 2 compared to 48 \pm 28.4 minutes in Group 1 ($p > 0.05$).

All patients in Group 1 had tachycardia as shown by a heart rate above 90 beats per minute. This was severe enough to require the use of labetalol in one instance. No patient had hypertension in this group.

Only 3 patients of the remifentanil group had a heart rate above 90 beats per minute. This was not high enough to require therapy. Blood pressure tended to be well maintained within a MAP of 100 mmHg. (Table 3) Respiratory depression, requiring the use of respiratory stimulants was present in all patients who had alfentanil (Table 3).

Table 3 Comparison of the efficacy of alfentanil and remifentanil in anaesthesia

	Alfentanil (Group 1)	Remifentanil (Group 2)
Tracheal extubation (min)	48 \pm 28.4	22 \pm 7.02
Haemodynamic response (HR>90)	100%	27%
Respiratory depression (Naloxone/doxapram used)	100%	18%

Values are mean \pm SD or percentages of patients with response.

There was no statistically significant difference in tracheal extubation time.

Interpatient variations in times to tracheal extubation were smaller with Group 2 (Figure 1).

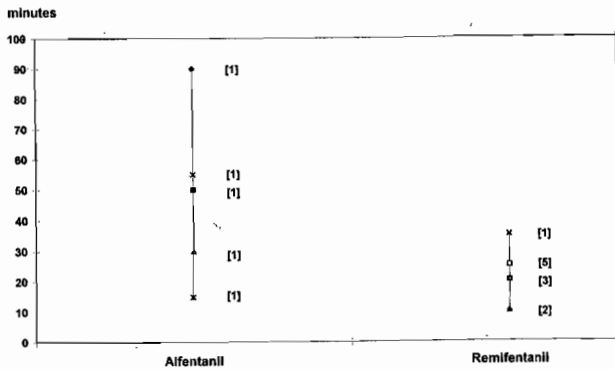


Fig. 1 Comparison of extubation times for patients on Alfentanil and Remifentanil

Discussion

We have compared alfentanil and remifentanil use as TIVA for spinal surgery. We have been able to demonstrate that remifentanil leads to a faster onset of recovery than alfentanil. Remifentanil also provides better haemodynamic stability than alfentanil without excessive hypotension ($P > 0.05$). This is especially important in patients with acute systemic insult to the spinal cord in whom prolonged hypotensive periods may further damage an already compromised spinal cord. Conversely, MAPs greater than 120mmHg may cause extensive haemorrhagic insult.

The total number of patients reviewed are small. This was due to the small number of patients presenting with spinal cord injury. The number would have been higher if we did not exclude five from the alfentanil group because they had ketamine in addition to alfentanil.

Remifentanil, a new member of the fentanyl family, is the first ultra-short acting opioid which can be rapidly titrated and individualized for various levels of surgical stimuli.

This study has confirmed other clinical studies comparing heart rate and systemic arterial pressure in groups of patients given remifentanil and alfentanil for analgesia in the balanced anaesthetic technique that there were consistently fewer untoward responses under remifentanil in the doses used^{1,2}.

In a study comparing the use of the two drugs in neuroanaesthesia, however no significant benefit could be demonstrated in terms of recovery from anaesthesia¹.

Monitoring of both sensory and motor evoked potentials has become an established part of successful spinal cord surgery³. Both the stimulus pattern and the anaesthetic technique are critical to the recording of reproducible motor potentials. Responses recorded from the cerebral cortex are more anaesthetic sensitive (particularly to nitrous oxide and the halogenated agents). Using a total intravenous technique with methohexitone and opioids such as alfentanil or remifentanil and an intubating dose of muscle relax-

ants, stable intraoperative motor evoked potential monitoring is now possible.

The choice of methohexitone as the induction agent in this series was based on its success during the process of comparison of various induction agents for use during spinal cord surgery at this centre³. The dose selected was based on a few published data³. The decision on whether or not to step down the dose at any time during surgery was purely clinical, based on the patient's physiological responses. Compared with propofol and various inhalational agents which are powerful suppressants of both magnetic and electrical transcranial evoked potentials, methohexitone allows for non-invasive monitoring of spinal motor tract integrity. It also causes less hypotension than propofol.

The use of alfentanil was consistently associated with tachycardia. This was severe enough to require the use of labetalol in one instance. Hypertension was however not present in this series. Respiratory depression, requiring the use of respiratory stimulants to suppress, was present in all patients who had alfentanil. This may have been due to the cumulative effects of alfentanil, as the patients had lower doses of methohexitone.

Our experience here indicates that remifentanil provides better flexibility of use with less tachycardia and respiratory depression than alfentanil for spinal cord surgery. Times to awakening and tracheal extubation were more predictable in patients receiving remifentanil which may be important if the goal is to awaken and tracheally extubate the patient in the operating room.

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