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Original Article

A Comparative Study of Remifentanil/Propofol versus Alfentanil/Propofol for Wake-up Test in Major Spinal Surgery

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Abstract

Background: Early warning of potential damage to spinal cord during major spinal surgery is highly desirable to prevent post-operative neurological deficits. Wake-up test is a simple, safe and reliable method of recognition of such a complication, and has been extensively used in many spinal surgical units. The present study is evaluating the remifentanil, propofol versus alfentanil, propofol as a part of balanced anesthesia for rapid performance of wake-up test during major spinal surgery.

Methods: Fifty patients undergoing elective spinal surgery were randomized to receive either remifentanil/propofol (group A) or alfentanil/propofol (group B). Premedicated patients received remifentanil (a loading dose of 2 μg/kg and a continuous infusion of 1 μg/kg/min), or alfentanil (a loading dose of 25 μg/kg and a continuous infusion of 1 μg/kg/min). Propofol was given as a loading dose of 1.5 mg/kg and a continuous infusion of 100 μg/kg/min.
The awakening was accomplished by withdrawing propofol and N_2O at 20 and 5 minutes before the test, respectively, whereas remifentanil or alfentanil infusion continued through the wake-up period at a rate of 0.02 ug/kg/min.

Results: The onset of intra-operative neurological examination in remifentanil/propofol receiving group (4.6±1.4 minutes) was significantly faster than that for alfentanil/propofol receiving group (7.5±1.8 minutes).

Conclusion: Combination of remifentanil and propofol induced a balanced anesthesia for intra-operative awakening and provided a faster opportunity for detecting any potential damage that may occur during spinal instrumentation.
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Keywords ● Surgery ● spinal cord monitoring ● analgesics ● remifentanil ● alfentanil

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Introduction

Intra-operative monitoring of spinal cord function is important during the correction of spinal curvature, placing pedicle screws or other spinal instrumentation. Distraction of spine may lead to ischemia of the spinal cord, as anterior spinal artery flow may be compromised.[1] Early warning of potential damage is highly desirable.

Two main methods including intra-operative somatosensory evoked potentials (SSEP) and wake-up test are currently used to detect spinal injuries.[2] The SSEP monitoring requires expensive equipments and trained technicians. The SSEP method is associated with artifacts as well as false positive and false negative results.[3] On the other hand, the wake-up test does not require any special apparatus, but should be performed by a skilled anesthesiologist.[4] An anesthetic agent that is associated with a faster recovery from anesthesia allows a more rapid assessment of a patient for wake-up test.

Alfentanil is the shortest-acting opioid available to anesthesiologists. But more recently another opioid, namely remifentanil, is introduced with its biological half-life being three to five minutes.[5-8] Although, these drug are used more frequently, there is no agreement about their effects on intra-operative analgesia, recovery, and awareness under anesthesia.[9,10] Therefore, the present study was conducted to compare the effects of remifentanil with alfentanil for the rapid assessment of patients in the wake-up test during major spinal surgeries.

Patients and Methods

The study was conducted as randomized and double-blind in spine surgical unit of Shahid Chamran Hospital of Shiraz University of Medical Sciences. The study included 50 male and female patients (16 to 70 years-old) with American Society of Anesthesiologists physical status I-II, referring to the hospital for elective major spinal surgery including scoliosis corrective surgery and vertebral fracture fixation.

Prior to the operations, all the patients were informed that they would be awakened during the operations, and would be asked to first move their hands and then their feet. They were assured that they would feel no pain whatsoever, and would be re-anesthetized quickly. A written consent to the procedure was obtained from each patient.

In all cases posterior spinal fusion was performed with Diapason by the same spine surgeon. Exclusion criteria were if patients were morbidly obese, hypersensitive to opioids, or chronic users of opioids, benzodiazepines, tricyclic antidepressants or anticonvulsants. Patients were randomly assigned to receive remifentanil/propofol (group A) or receiving alfentanil/propofol (group B).

Based on patients' weights, an anesthetist prepared the drug solutions in syringes for bolus and infusion labeled with dose volume or rate of infusion. To maintain blinding of the study, the volumes (ml) and rates of infusion (ml/hour) for both groups were identical, and drug administrations were performed by a different anesthetist.

Patients were premedicated with diazepam (0.1 mg/kg, PO) and atropine sulfate (0.01 mg/kg, IM). Afterwards, intravenous catheters, ECG leads, noninvasive blood pressure cuff, capnography, and pulse oximeter were paced. Radial artery catheter was also placed for continuous monitoring of arterial blood pressure. The patients were then anesthetized followed by insertion of Foley's catheters. Prior to the induction of anesthesia, patients breathed 100% oxygen for 3 minutes and received an infusion (5 ml/kg) of lactated ringer solution intravenously.

Anesthesia was induced using a bolus (given over 60-90 seconds) of remifentanil (2 μg/kg) or alfentanil (25 μg/kg). A continuous infusion (1 μg/kg/min) of each drug was then started in both groups. At first propofol was administered at 1.5 mg/kg (10 mg every 10 seconds) followed by continuous infusion of 100 μg/kg/min. Patients then received 0.6 mg/kg atracurium to facilitate oro-tracheal intubation. After intubation the patients were ventilated mechanically with a gas mixture of 50% nitrous oxide in oxygen. To maintain an appropriate level of anesthesia during surgery, the infusion rate of remifentanil or alfentanil was reduced to 0.5-1 μg/kg/min starting at 5 minutes after intubation.

Deliberate hypotension was provided throughout the surgery to maintain a mean arterial blood pressure of 50-55 mmHg by continuous infusion of sodium nitroprusside (0.5-3 μg/kg/min). 30 minutes before execution of the wake-up test, the recovery from neuromuscular block was checked by transcutaneous train of four stimulation of ulnar never at the wrist (two or three twitches). Then the infusion of propofol and inhalation of nitrous oxide were then discontinued at 20 and 5 minutes before the awakening test. During the test the patients received 100% oxygen with either remifentanil or alfentanil at an analgesic rate of 0.02 μg/kg/min. The patients were then called by their first name, asked to move their hands, and then they were required to move their both feet. After the test, patients were re-anesthetized with a bolus of propofol (1 mg/kg), followed by an infusion of propofol (100 μg/kg/min). The administration of remifentanil, alfentanil and nitrous oxide were resumed to the pretest levels, and supplemental doses of muscle relaxant were given if required.

At the end of the surgical procedures, muscle relaxation was reversed by neostigmine (2.5 mg) and atropine (1.25 mg). Then the rate of infusion of remifentanil and alfentanil was reduced to 0.02 μg/kg/min. When an adequate spontaneous respiration established an intravenous injection of

morphine (0.1 mg/kg) was performed. Fifteen minutes after the administration of morphine, the infusion of remifentanil and alfentanil was discontinued, and the patients were transferred to a recovery room, where blood pressure, heart rate and oxygen saturation (SPO_2) were monitored for up to three hours. At the end all of the patients were interviewed regarding intra-operative and wake-up test recalls before and 24 hrs after discharge from recovery room.

Statistical analyses

The quantitative data, shown as mean±SD, were analyzed using unpaired Students *t* test, and Fisher's exact tests. *P*<0.05 was considered as statistically significant.

Results

Patient's characteristics are summarized in Table 1. Overall, no significant differences were found between two groups regarding sex, age and weight. The duration of intra-operative wake-up test that was the movements of patients' feet in response to verbal command are presented in Table 2. This duration in group A was 4.6±1.4 min which was significantly shorter than that of group B (7.5±1.9 min).

Table 1: Demographic data of patients

Data	Group A	Group B
Sex ($^M/_F$)	16/9	14/11
Age (yrs)	28.0±9.7	22.0±11.3
Weight (Kg)	65.0±13.3	57.4±13.4

Table 2: Time interval (minutes) between verbal command and patient's response in wake-up test.

Wake-up time	Group A	Group B
Mean (min)	4.60 ± 1.39	7.48±1.85
Range (min)	2-7	5-10

There was no significant difference between mean arterial blood pressure and heart rate before or during wake-up test in the two groups (Table 3).There was no significant difference between the numbers of patients recalling events during wake-up test of both groups. None of the patients consider the events as painful. None of the patients remembered intraoperative events before and after the wake-up test, Table 4.

Table 4: The number and percentage of patients showing awareness during the operations and wake-up test.

Recall during	Group A n=25	Group B n=25	P value
Operation	0 (0%)	0 (0%)	—
Wake-up test	6 (24%)	4 (16%)	0.363

Discussion

Damage to the spinal cord and subsequent paraplegia is a recognized and most feared complication of the major spinal surgeries.[1-4] Wake-up test is a simple, safe and reliable method of the recognition of such a complication.[3] It has become increasingly important to find the anesthetic or the combination of anesthetics that, while provides appropriate analgesia and amnesia for the surgical procedure, allows a more rapid assessment of the patient for wake-up test. Therefore, the present study was designed to compare the effects of two ultra-short acting opioids, namely remifentanil and alfentanil, on the time required for wake-up test in patients under balanced anesthesia subjected to a spinal surgery. The doses of such drugs were conventional and meant to reflect those used or suggested for use in clinical practice.

The terminal elimination half-life of remifentanil is less than 10 minutes, and is rapidly metabolized to inactive metabolites by non specific blood and tissue esterases.[5] Alfentanil is also a potent and short acting narcotic analgesic chemically related to fentanyl. The duration of action of alfentanil is only one third of that of an equi analgesic dose of fentanyl. The average of terminal elimination half-life of alfentanil is 83-223 minutes and is mainly metabolized by the liver to inactive metabolites.[12]

Schuttler and colleagues showed that compared to alfentanil, remifentanil provided a better intra operative hemodynamic stability during major abdominal surgeries in patients under balanced anesthesia with 0.5% end tidal isoflurane and 60% nitrous oxide as well as a faster recovery from anesthesia.[13] However, there is no superiority of remifentanil over alfentanil with respect to immediate post-operative recovery from anesthesia for out patient surgery or the time of patient's response to verbal command.[14] Rodola and colleagues, on the other hand, studied the

Table 3: the mean±SD values of mean arterial pressure (MAP) and heart rate (HR) before and during the wake-up test.

	MAP (mmHg)			HR (bits/min)		
Wake-up test	Group A	Group B	P value	Group A	Group B	P value
Before	64.9±7.7	66.0 ± 7.1	0.395	54.8 ± 3.4	54.8 ± 2.7	1.000
During	72.2 ± 6.2	74.1 ± 6.5	0.287	71.2 ±13.6	69.7±13.9	0.706

effectiveness of remifentanil balanced anesthesia for wake-up test in major spinal surgery, showed that intraoperative neurological examination was possible in 4-6 minutes with only negligible changes in hemodynamics during the test.[11] They also reported that two out of 10 patients remembered the procedure but did not regard it as painful or disagreeable.[11] In the present study, following the mean results of wake-up test in group A was 4.6±1.4 min which was significantly shorter than of group B (7.5±1.8 min).

A protocol allowing the performance of wake-up test in a shorter period, even for one minute, and hence preventing the catastrophic complication of paraplegia in major spinal surgery is crucial and can not be hidden from any anesthetist and surgeon involved in spinal surgery. The findings of the present study indicate the superiority of remifentanil/propofol anesthetic technique. This advantage of remifentanil over alfentanil is due to context–sensitivity of half-time (the time for the effect site concentration of a drug to fall 50% after a variable length infusion) of the two drugs. Remifentanil has a constant context–sensitive half-time of 3-5 minute, which is independent of the duration of infusion.[7,12] Whereas, the half-time of alfentanil after 1 minute infusion increases from one minute to 40 minutes after 1 hour infusion and to 60 minutes after 4 hour infusion.[7-14]

Conclusion

It seems that remifentanil / propofol balanced anesthesia is advantageous over alfentanil/propofol balanced anesthesia procedure, in regard to performing wake-up test in shortest period.

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