Remifentanil *vs* Morphine for Patients in Intensive Care Unit Who Need Short-Term Mechanical Ventilation

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Abstract

This randomized, double-blind study compared the safety and efficacy of remifentanil (9 μg/kg/h) with morphine (0.045 mg/kg/h plus a bolus dose of 0.025 mg/kg). One hundred and eighty nine Intensive Care Unit (ICU) patients with normal renal function or mild renal impairment requiring mechanical ventilation were included in this study. A pre-defined dosing algorithm permitted initial titration of the opioids to predetermine the optimal level of sedation and pain score. Supplementary infusion of midazolam (0.03 mg/kg/h) was given when additional sedation was required. The duration of optimal sedation during the maintenance phase was 82.7 per cent and 84.3 per cent of the total time in the remifentanil and morphine groups respectively. There were no statistically significant differences in the between-subject variability in the duration of optimal sedation between the two treatment groups. Midazolam was not required in approximately 75 per cent of all patients. The patients in the morphine group required twice the amount of midazolam required by the remifentanil group. The dosing algorithm facilitated rapid extubation in both groups. Remifentanil provided comparable hemodynamic stability to morphine, and was not associated with an increase in cardiovascular adverse event. Remifentanil is therefore considered to be effective and well tolerated in ICU patients.

Key word : Intensive Care Unit, Mechanical Ventilation, Sedation and Analgesia, Remifentanil, Morphine

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To achieve optimal medical care, critically ill or injured patients require a combination of analgesia and sedation during their stay in the ICU. This is normally provided by opioids and benzodiazepine. The elimination of these opioids may be prolonged in critically ill patients due to the potential for accumulation, resulting in unpredictable and/or delayed recovery particularly during weaning from mechanical ventilation. Agents such as midazolam and propofol have gained wide acceptance in the ICU as the sedative component because of their effectiveness and short elimination half-life[1,2].

Remifentanil hydrochloride is a selective mu-opioid receptor agonist, metabolized by nonspecific esterases in the blood and tissues[3] which results in a short effective biological half-life of less than 10 minutes and has no accumulation after prolonged infusion[4]. The titration and predictable effect of remifentanil offers potential clinical advantages over the existing opioids for use in combined analgesia and sedation[5,6]. Many studies have already been published describing the potential role [7] and actual use of remifentanil in the general ICU [8-10] and neurosurgical ICU[11] setting.

The objectives of this study were to compare the effectiveness and safety of a remifentanil-based regimen with a morphine-based regimen by comparing the mean percentage of hours of optimal sedation and pain control, the time between starting the extubation process and actual extubation, hemodynamic profiles, adverse event, mean infusion rates, and the incidence of supplementary open-label midazolam and open-label morphine bolus doses administered for stimulating procedures or rescue.

MATERIAL AND METHOD

Study design

The study was a randomized, double-blind, parallel-group, multi-national, multi-center study comparing a remifentanil-based regimen with a morphine-based regimen in post-surgical and medical ICU patients requiring sedation during short-term mechanical ventilation for at least 12 hours up to 72 hours. This study was done in eight countries, with twenty study sites.

Study procedures

The main part of this study was double-blind and the randomization of the treatment regimen was stratified according to the type of patients (ie post-cardiac surgery, post-general surgery, medical problem), the patients' modified ICU admission Simplified Acute Physiology Score (SAPS II)[12] and renal function. Efficacy was investigated by assessing the level of sedation and pain scores at regular interval. Sedation was assessed using the Sedation Agitation Scale (SAS)[13]. The effectiveness of the two treatment regimens was assessed by investigating the ability to maintain an SAS score of 4 with no or mild pain. The six-point pain intensity scale was used during this study. Clinically significant pain was defined as a score of equal to or more than 3.

The Vancouver Interaction and Calmness Scale[14] was also used as a secondary assessment of sedation. At the completion of this task, the overall Interaction and Calmness scores were calculated by adding up the individual scores to each of the assessments.

This study was divided into four period:

Screening period

Patients who were likely to or were actually receiving mechanical ventilation *via* an orotracheal tube for at least 12 hours up to 72 hours were included in the study. Serum creatinine was studied and predicted creatinine clearance was then calculated[15].

Treatment period

The treatment period started from the time the study drug was administered until the study drug was discontinued. This period was composed of three phases: maintenance, extubation, and post-extubation phases.

Maintenance phase

This phase began from the administration of the study drug to the time when the extubation phase was begun. The study drug was started when the SAS score was equal to or more than 2. Patients received a 6 ml/h infusion of the study drug which was 9 μg/kg/h (0.15 μg/kg/min) of remifentanil[16-18] or 0.045 mg/kg/h (0.00075 mg/kg/min) of morphine[19] with a simultaneous 5 ml analgesic bolus dose administered over 60 seconds. The infusion rate was titrated every 20 minutes to provide optimal sedation with no or mild pain. When the study drug had reached the midazolam "trigger dose", then an infusion of midazolam was stated at a rate of 0.03 mg/kg/h to supplement sedation. The study drug infusion could be titrated up to a maximum of 40 ml/h (remifentanil dose 60 μg/kg/h or 1 μg/kg/min; morphine dose 0.3 mg/kg/h or 0.005 mg/kg/min). Midazolam could be

titrated up to a maximum dose of 0.2 mg/kg/h. All parameters were recorded every 20 minutes for the first six hours and every hour until the extubation phase was begun.

Extubation phase

The extubation phase consisted of the time that the extubation process began until the time of actual extubation. At the time that the decision was made, the midazolam infusion was then stopped. The study drug infusion syringe was replaced in a blinded "syringe swap", so that remifentanil patients would receive a further infusion of remifentanil, whilst morphine patients received a placebo infusion. The study drugs were simultaneously reduced to 4 ml/h.

Post-extubation phase

This phase started from the time that the subject was extubated until the study drug was discontinued. Immediately following extubation, the infusion was reduced by 25 per cent every 20 minutes until completion.

Post-treatment period

The post-treatment period started from the time the study drug was discontinued until 24 hours later or until ICU discharge or death.

Follow-up period

The follow-up period started from 24 hours after the completion of the study drug until the patient was discharged from ICU or the end of day 7 or death.

Study population

Patients were screened as soon as they entered the ICU. Inclusion criteria were; admitted to the ICU within the previous 24 hours, intubated and expected to require short-term mechanical ventilation, aged more than 18 years old, female patients should be non-childbearing, weight less than 120 kg, and informed consent should be obtained prior to participation in the study. Exclusion criteria were patients who had concurrent treatments such as neuromuscular blocking agents or had received an epidural block during the maintenance phase, or had concurrent disease or disorders including those likely to require tracheostomy within 96 hours, had a neurological disease or other medical condition that may have affected the ability to assess sedation and pain levels, history of allergic hypersensitivity or contraindications to remifentanil, morphine or benzodiazepines, had a history of drug abuse including alcohol. Patients with a predicted CCr more than 80 ml/min was defined as having normal renal function. If the predicted CCr was 50-80 ml/min, this was defined as mild renal impairment.

Criteria for premature study drug and/or study discontinuation

At any time during the study, if the patient's safety was compromized or continuation of the treatment regimen was inappropriate for ongoing clinical management, the investigator could discontinue the study treatment and proceed with appropriate standard therapy for that patient.

Sample size considerations

A total of 189 subjects were recruited: 13 patients in the pilot phase (8 in remifentanil group and 5 in morphine group), 24 patients were included in practice phase (all patients received remifentanil), and 152 patients were in the double-blind phase and were randomized to 74 patients in remifentanil group and 78 patients in morphine group. Due to the nature of the pilot and practice phase, the data of these patients were not included in any of the efficacy analyses but were included in the safety analyses.

Intent-To-Treat (ITT) population

All randomized double-blind patients who had received any dose of the study drug and had at least one post-dose efficacy measurement were included. The ITT population was the primary effective population and was included in all efficacy analyses. Open-label pilot and practice patients were not included in the ITT population.

Statistical analysis

Summary statistical computations were performed using SPSS version 6.12 on UNIX. Dichotomous and categorical variables e.g. female patients were presented as number or percentage. Discrete counts, e.g. number of times the infusion rate was increased were presented as frequency distributions. The number of patients with non-missing values accompanied by the mean, median, standard deviation, and range were used to summarize continuous

values. All percentages were based on patients with recorded data. All tests of significance were two-sided and carried out at the 5 per cent level.

RESULTS

Subject accountability

One hundred and eighty-nine patients were recruited in this study with 152 double-blind patients (74 in remifentanil group and 78 in morphine group) (Table 1). Eighty-eight of them were post-general surgical patients; sixty-two were post- cardiac surgical patients and two medical patients. Sixty-five patients in the remifentanil group and forty-nine patients in the morphine group had normal renal function. The others had mild renal impairment.

Demographic characteristics were well matched indicating a similar case mix of patients in both groups. Baseline values in the double-blind patients such as SAS score, Pain Intensity score (PI) and hemodynamic parameters were also similar at the begining of the study (Table 2). The duration of infusion of the study drugs at all study phases was in the same range (Table 3). Eighteen patients were prematurely discontinued (8 in the remifentanil group, 10 in the morphine group). Most of them were as a result of major adverse events caused by surgical or other medical problems. There were only two patients (one in each group) that were discontinued as a result of the study drugs.

There were 5 major violations (3 in remifentanil group and 2 in morphine group) (Table 1). All of them were excluded from the final analysis. One patient in the morphine group failed to achieve an SAS score of 4 from the start of the study drug until the end of the evaluation.

Efficacy

Analysis of the primary end point showed that there was no significant difference in the between-subject variability in the proportion of time that the patients were optimally sedated between remifentanil and morphine regimens (Table 4). There was no significant difference in the duration of optimal sedation with mild or no pain (Table 5, 6). The mean infusion rate for maintenance of remifentanil and morphine were 8.6 ± 0.14 (3.5-13.0) μg/kg/min and ± 0.049 (0.024-0.091) μg/kg/min respectively.

The numbers of patients in each group that were optimally sedated without the use of midazolam were similar (78% of patients in remifentanil group and 73% of patients in morphine group). But the patients in the morphine group required approximately twice the amount of midazolam compared with the remifentanil group (median total midazolam dose was 28.4 mg in morphine patient and 15.0 mg in remifentanil patient).

The mean and median times of the extubation phase were similar in both groups. Two patients

Table 1. Study population, type of subject and reasons of premature discontinuation.

Study population	Remifentanil	Morphine	Total
Total number of safety population	**106**	**83**	**189**
- pilot patients	8	5	13
- practiced patients	24	-	24
- double blind patients	74	78	152
type of patients			
- post general surgery	43	45	88
- post cardiac surgery	30	32	62
- medical problem	1	1	2
Premature discontinuation	**8**	**10**	**18**
- adverse events	6	6	-
- practical problems	1	2	-
- renal impairment	1	1	-
- other	-	1	-
Major violation	**3**	**2**	**5**
Cause			
- lack of efficacy	-	1	-
- patient received medication that interfered with the interpretation of primary efficacy	3	1	-

Table 2. Baseline clinical characteristics before infusion of the study drug.

Clinical Characteristics	Safety population		Double-blind population	
	Remifentanil n=106	Morphine n=83	Remifentanil n=74	Morphine n=78
Age (yr)	58.3 ± 15.3 (18-84)	66.3 ± 14 (20-85)	58.8 ± 14 (19-80)	59.9 ± 14.2 (20-85)
Weight (kg)	70.8 ± 14.8 (45.5-120)	71.4 ± 17.6 (39-118)	71.4 ± 16 (45.5-120)	71.0 ± 17.8 (39-118)
Height (cm)	166.5 ± 9.1 (145-185)	167.2 ± 8.6 (150-185)	167.3 ± 9.3 (145-185)	167.2 ± 8.7 (150-185)
Sex (men/women)	35/71	30/53	22/52	27/51
Race				
- White	78	61	54	56
- Black	4	4	4	4
- Asian	23	18	19	18
- Other	1	-	-	-
SAPS II			25.8 ± 9.6 (6-49)	25.6 ± 8.5 (6-52)
SAS			3.5 ± 1.1 (2-5)	3.4 ± 1.1 (2-5)
PI			1.9 ± 1.1 (1-5)	1.6 ± 1.1 (1-5)
MAP			88.5 ± 17.8 (52.7-130.3)	89.3 ± 17.7 (60.3-132.3)
HR			90.1 ± 19.8 (58.1-142.5)	90.9 ± 17.4 (65.1-131.5)

Data are means ± SD (range) or numbers (*n*).
SAP II = simplified acute physiology score, SAS = sedation agitation score,
PI = pain intensity score, MAP = mean arterial pressure (mmHg), HR = heart rate (beats/min).

Table 3. Duration of study phases compared between groups.

Duration (hours)	Remifentanil (n=74)	Morphine (n=78)
ICU entry to start of study drug	3.01 ± 1.1 (2.0-23.8)	3.04 ± 1.0 (1.8-19.4)
Maintenance phase	15.7 ± 9.7 (4.1-73)	14.4 ± 7.5 (1.7-55.5)
Extubation phase	1.5 ± 1.9 (0-11.5)	2.5 ± 4 (0-23.8)
Post extubation phase	0.8 ± 0.4 (0-1.5)	0.9 ± 0.3 (0-1.3)
Post treatment period	13.7 ± 10.1 (0-24)	14.7 ± 9.9 (1-24)

Data are means ± SD (range).
There were no statistically significant differences.

in morphine group were apnoeic during the extubation phase that led to premature discontinuation of the study drug. However both of them could be extubated within the same time range as the others.

The proportion of time that patients experienced pain during extubation and post-extubation phases was statistically significantly longer in the remifentanil group. This is consistent with the rapid offset of the effects of remifentanil.

Safety

There was no statistically significant difference between the percentage of patients with overall adverse events (40% in remifentanil and 39% in morphine group) and with drug-related adverse events (22% in remifentanil and 16% in morphine group) in both groups. The overall number of patients with adverse events leading to permanent discontinuation of the study drug during the maintenance phase was also not significantly different in both groups.

The incidence of serious adverse events was higher in the remifentinil group (7% in remifentanil and 4% in morphine group) but this was not statistically significant. There was only one patient in the remifentanil group who had a serious adverse event which was considered to be possibly related to the study drug.

Three deaths (2 in remifentanil group and 1 in morphine group) were reported during the study. None of the deaths was considered by the investigator to be possibly related to the study drug.

Table 4. Percentage of hours of optimal sedation during the study period and treatment phase.

	Remifentanil (n=74)	Morphine (n=78)
Maintenance phase	82.7 (4.7-100.0)	84.3 (0.0-100.0)
Extubation phase	93.1 (32.8-100.0)	95.8 (0.0-100.0)
Post extubation phase	95.5 (33.3-100.0)	98.3 (63.3-00.0)
Post treatment peroid	93.8 (0.0-100.0)	93.2 (0.0-100.0)

Data are means (range).
There were no statistically significant differences.

Table 5. Percentage of hours by degree of sedation compared between groups.

	Remifentanil (n=74)	Morphine (n=78)
SAS score 1	0.2 (0-7.1)	0.1 (0.0-4.3)
SAS score 2, 3	13.1 (0.0-95.3)	12.7 (0.0-100.0)
SAS score 4	82.7 (4.7-100.0)	84.3 (0.0-100.0)
SAS score 5, 6	4.2 (0.0-52.8)	3.0 (0.0-19.0)
SAS score 7	0	0

Data are means (range).
There were no statistically significant differences.
SAS = sedation agitation score.
SAS score 1 = unarousable
SAS score 2, 3 = excessively sedated
SAS score 4 = optimally sedated
SAS score 5, 6 = inadequately sedated
SAS score 7 = dangerous agitated

Other safety results

Mean arterial blood pressure (MAP) during and after treatment

The MAP during the maintenance phase was lower than the baseline value in the remifentanil group but the difference was small and not clinically significant. The MAP of the patients in the remifentanil group during the extubation phase, post-extubation phase, and post-treatment period were significantly higher than patients in morphine group. More patients in the remifentanil group had a MAP≥100 mmHg.

Respiratory rates (RR)

Respiratory function summaries were produced on the subset of subjects who were extubated within 73 hours of the start of the study drug (Table 7). There were significantly fewer patients in the remifentanil group who had a RR 10 bpm (p=0.042).

Mean fractional inspired oxygen concentration (FiO_2) and mean peripheral oxygen saturation (SpO_2) values at scheduled time points were not statistically significantly different.

DISCUSSION

The aim of this study was to compare the safety and efficacy of a remifentanil-based regimen and a morphine-based regimen, supplemented where necessary with midazolam, for providing analgesia and sedation during mechanical ventilation in the ICU. To achieve a balanced mixture of patients in the two treatment groups, randomization of the treatment was stratified by the type of subject and by each patient's modified ICU admission SAPS II. This approach was proved to be very effective since the characteristics of the two treatment groups were well matched.

The dosing algorithm used in this study was designed to mimic a standard morphine/midazolam regimen as well as allow titration of the opioid infusions, in the first instance, to achieve and maintain optimal sedation. It was expected that morphine

Table 6. Percentage of hours in which the patients had no pain or mild pain.

	Remifentanil (n=74)	Morphine (n=78)
Maintenance phase	94.5 (2.9-100.0)	93.9 (4.5-100.0)
Extubation phase	93.3 (0.0-100.0)	95.3 (0.0-100.0)
Post extubation phase	81.8 (0.0-100.0)	95.5 (0.0-100.0)
Post treatment peroid	87.6 (0.0-100.0)	95.8 (16.7-100.0)

Data are means (range).
There were no statistically significant differences.

Table 7. Respiratory rate during the extubation process.

	Remifentanil	Morphine	P- value
Number of patients (%) with RR<10 bpm	4 (4%)	10 (13%)	0.042
Number of patients (%) with RR>20 bpm	69 (71%)	49 (64%)	NS
Time of RR<10 bpm			
- mean percentage	0.7	1.5	ND
- range	0.0-37.0	0.0-30.8	ND
Time of RR>20 bpm			
- mean percentage	36.0	26.1	ND
- range	0.0-100.0	0.0-100.0	ND

RR = respiratory rate, NS = no statistically significance, ND = not done.

treated patients would receive more midazolam due to the administration of a lower dose. However, using this dosing algorithm, both remifentanil and morphine were very effective at providing optimal sedation without the need for the addition of midazolam in the majority of the patients. This reflects the stringent conditions of the dosing algorithm, frequent monitoring, and adjustment of the level of sedation to ensure that a SAS score of 4 was maintained. The SAS score targeted in this study resulted in a lighter level of sedation than is normally used in the clinic and resulted in a reduced requirement for midazolam. In routine clinical practice, subjects are likely to be less frequently monitored and more deeply sedated, especially during the night. Without constant monitoring of the subject's SAS score, there is a potential for conventional opioids such as morphine to accumulate. The high overall percentage of time with optimal sedation observed in this study is very similar to other reports[1,2,20].

The target Ramsey score of 2-5 used by Carrasco, et al. is less stringent than the SAS score 4 used in the present study. Analysis of the primary end point using data from all the patients in the ITT population demonstrated that there was no statistically significant difference in the variability in the proportion of time that subjects were optimally sedated between the remifentanil and morphine regimens. The primary end point analysis was repeated to evaluate the variability from the time that the subject first achieved a SAS = 4 and found no statistically significant difference. The lack of difference in the variability is likely to be a result of the longer time interval between assessments following a change in opioid dosing. The 20-minute interval was based upon the pharmacokinetic profile of morphine and represented the time needed to observe the effects of a bolus dose and change in the infusion rate. The majority of the effects of changing the remifentanil infusion would be seen in less than 10 minutes, however, the longer time frame was adopted for both treatment groups to allow a fair comparison and to ensure integrity of the study blind was maintained. Extending the re-assessment time in the remifentanil group may have resulted in a delay in the response to changes in analgesia/sedation requirements and therefore introduced more variability in the remifentanil group.

However, the 20-minute reassessment time incorporated into the algorithm was proved to be a

clinically adequate for effective provision of analgesia and sedation since very few subjects needed to receive rescue medication. There was a trend for less remifentanil subjects to receive a midazolam bolus as rescue medication compared with morphine subjects and was an indication that the dosing algorithm was effective.

All patients in this study were carefully monitored and were under light levels of sedation so the time to extubation for the morphine patients were not prolonged. This is unlikely to have been the case for the remifentanil patients due to its predictable offset of action, which is independent of the duration of infusion. Wilhelm, et al[10] have recently demonstrated that two-thirds of ICU patients who receivied remifentanil were extubated within 15 minutes of starting the extubation process and 87 per cent by 45 minutes.

Less than 30 per cent of the patients in either treatment group required the midazolam infusion to be started. The midazolam infusion was started sooner in morphine patients, and more morphine patients required a midazolam bolus dose which resulted in the overall median total midazolam dose in the morphine group being nearly twice that of remifentanil group. Although this difference was not statistically significant, it is indicative of a trend towards reduction of midazolam requirement in the remifentanil group.

The proportion of time that patients experienced at least moderate pain was similar during the maintenance and extubation phases, but significantly more pain was felt by the remifentanil group during the post-extubation phase and post-treatment period. More patients in the remifentanil group received either morphine or midazolam during the extubation or post-extubation phase of the study and this is to be considered consistent with the rapid offset of the effects of remifentanil.

Safety

The incidence of adverse events was comparable between the two treatment groups and within the different treatment phases except that there was a higher incidence in the morphine group during the post-treatment period. The events mainly involved the digestive tract (nausea, vomiting; three subjects) and two cases of drug-related respiratory depression.

There was a similar incidence of serious adverse events in the remifentanil group and only one event (hypotension) was considered drug-related. The differences between treatment groups were not statistically significant. These events were typical for subjects in the ICU and those receiving a mu-opioid agonist. The majority of the adverse events leading to discontinuation of study drug were considered to be severe at the time of discontinuation. However there was no consistent pattern to the nature of the adverse events leading to permanent discontinuation of study drug within and between the two treatment groups.

There was a statistically significant difference in the proportion of patients with a MAP>100 mmHg in the remifentanil group during the post-extubation phase and post-treatment period and this was probably related to the higher incidence of pain after the maintenance phase, resulting in greater sympathetic drive in remifentanil patients. The overall data of MAP and heart rate indicated that remifentanil provided an acceptable degree of hemodynamic stability.

There was a statistically significant difference in weighted mean respiration rate between the treatment groups and a larger number of morphine patients had a respiratory rate<10 bpm during the post-extubation phase. These effects are likely to reflect the longer half-life of morphine producing a more pronounced effect an the respiratory center.

SUMMARY

A remifentanil-based regimen was as effective as a morphine-based regimen in the provision of optimal sedation and facilitation of rapid extubation in patient with normal renal function and mild renal impairment. Remifentanil provided good hemodynamic stability which was similar to that observed in patient received morphine. Remifentanil was well tolerated and the adverse events that occurred were not unexpected for intensive care patients receiving a potent mu-opioid agonist.

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การศึกษาเปรียบเทียบความสามารถในการสงบประสาทและควบคุมอาการปวดระหว่างการใช้ remifentanil ร่วมกับ midazolam กับการใช้ morphine ร่วมกับ midazolam สำหรับผู้ป่วยในหอผู้ป่วยหนัก ที่ต้องใช้เครื่องช่วยหายใจ

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การศึกษาเปรียบเทียบความปลอดภัยและประสิทธิผลของการใช้ยา remifentanil ในขนาด 9 ไมโครกรัม/กก/ชม กับมอร์ฟีน 0.045 มก/กก/ชม หยดเข้าหลอดเลือดดำ เพื่อควบคุมให้ผู้ป่วยสงบและไม่ปวดในผู้ป่วยซึ่งต้องใช้เครื่องช่วยหายใจและได้รับการดูแลอยู่ในหอผู้ป่วยหนัก โดยทำการศึกษาแบบสุ่ม และ double blind ในผู้ป่วยอาการหนัก 189 คน จาก 20 สถาบัน โดยผู้ป่วยจะได้รับ midazolam เมื่อเพิ่มปริมาณยาที่ทำการทดสอบถึงระดับที่กำหนดไว้และไม่สามารถควบคุมให้ผู้ป่วยสงบได้ ผลการศึกษาพบว่ายาทั้ง 2 ชนิดสามารถทำให้ผู้ป่วยสงบได้ถึงระดับที่ต้องการในระยะเวลาตลอดการศึกษาใกล้เคียงกัน และเมื่อผู้ป่วยสงบแล้วยาทั้ง 2 ชนิดก็สามารถควบคุมระดับการสงบได้ดีใกล้เคียงกันตลอดระยะเวลาที่ให้ยา ผู้ป่วยทั้ง 2 กลุ่มต้องการ midazolam เพื่อเสริมฤทธิ์การสงบไม่แตกต่างกัน แต่ผู้ป่วยกลุ่มที่ได้รับมอร์ฟีน ต้องการขนาดยา midazolam มากกว่ากลุ่ม remifentanil ผู้ป่วยทั้ง 2 กลุ่มสามารถฟื้นจากการสลบและถอดท่อหายใจได้ในเวลาใกล้เคียงกัน การใช้ remifentanil เป็นยาสงบประสาทไม่ทำให้มีการเปลี่ยนแปลงของความดันเลือด และอัตราเร็วของหัวใจเต้นแตกต่างจากการใช้มอร์ฟีน รวมทั้งไม่พบภาวะแทรกซ้อนของระบบไหลเวียนเลือดมากกว่าการใช้มอร์ฟีน

คำสำคัญ : หอผู้ป่วยหนัก, เครื่องช่วยหายใจ, สงบประสาทและระงับปวด, remifentanil, มอร์ฟีน

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