A Multicenter Randomized Double-Blind Comparison of Remifentanil and Alfentanil During Total Intravenous Anaesthesia for Out-Patient Laparoscopic Gynaecological Procedures

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Abstract

We compared Remifentanil, an esterase-metabolized opioid, with Alfentanil as part of the total intravenous anesthesia with propofol and atracurium for out-patient laparoscopic gynaecological procedures in a multicenter randomized, double-blind study. We chose Remifentanil 1 mg./kg.for bolus injection and a continuous infusion of 0.25-0.5 μg./kg./min, compared to Alfentanil 20 μg./kg. For bolus injection and a continuous infusion of 0.5-1 μg./kg./min. Fifty-nine patients received Remifentanil, and sixty-three received Alfentanil. Patients who received Remifetanil experienced significantly fewer stress responses to surgical stimuli ($p < 0.05$) and required fewer additional boluses of study drugs and propofol ($p < 0.05$) than Alfentanil during the intraoperative period. Response time to verbal commands, spontaneous respiration, adequate respiration and tracheal extubation, were not significantly different between these two opioids. Remifentanil patients, required more fentanyl for post operative pain control, 40 from 59 cases in the Remifentanil group and 22 from 63 cases in the Alfentanil group ($p < 0.05$) but still showed significantly better recovery of psychomotor function by Aldrete score of ten at 50 and 60 min ($p < 0.05$) than Alfentanil patients. The incidence of intraoperative bradycardia was significantly higher with Remifentanil. Other incidences of nausea, emesis, urinary retention and postural hypotension were similar. All patients were ready to be discharged from the hospital within two hours after extubation except for one patient in the Alfentanil group who needed five hours of hospital stay because of urinary retention, nausea and severe emesis.

Key word : Remifentanil, Total Intravenous Anaesthesia, Out-Patient

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Nowadays, there are many procedures that can be done in an out-patient setting including laparoscopic gynaecological procedures. These procedures are performed by inflating the abdominal cavity with carbon dioxide to increase the abdominal space for introducing the instruments. General anaesthesia can provide both unconscious and abdominal relaxation with reliable control of the arterial carbon dioxide level. Supplementary anaesthesia either with inhalation or intravenously can be done in combination or separately. Since intravenous agents cause less nausea and vomiting, it will shorten the duration of the postoperative period. The main problem is how to use opioids to give adequate intraoperative pain control with minimum postoperative sequelae that will cause an unexpected prolonged postoperative period. If postoperative pain control can be provided by the combination of local anaesthetic infiltration or preoperative non-steriodal anti-inflamatory drug administration, it will be beneficial to the patients.

Remifentanil is a new ultra-short acting, esterase-metabolised opioid. Because of its specific μ-agonist action, it is 20-30 times more potent than Alfen-tanil[1]. But it has the same onset, duration of action and effect on respiratory depression as Alfentanil and both can be reversed with naloxone. As an ester, Remifentanil is susceptible to hydrolysis by blood and tissue non-specific esterases, resulting in rapid half life, low context sensitivity half time[2], rapid recovery and low risk of cumu-lative effects regardless of the duration of infusion or the number of doses administered, even in patients with impaired renal function [3,4]. In general, the administered dose should be reduced in elderly patients[5,6]. A high dose of Remifentanil in patients on spontaneous ventilation can cause hypoventilation as seen with Alfentanil[7] but recovery of respiratory function is rapid once the infusion rate is decreased or stopped. Bolus injections of Remifentanil can induce bradycardia and hypotension during anaesthesia. In combination with benzodiazepine, Remifentanil enhances sedation and anxiolytic effects[8].

Both Alfentanil and Remifentanil have minimal depressive effects on the cardiovascular system[7,9] and are good choices for out-patient anaesthesia. There are many comparative studies between these two drugs but none in the single procedure for out patient anaesthesia. This study compares their effectiveness as a supplement of propofol in total intravenous anaesthesia for out-patient laparoscopic gynaecological procedures using a multicenter randomized control double blind study.

Objective

The primary objective of this study was to compare the recovery profile after total intravenous anaesthesia supplement with either Remifentanil or Alfentanil. The early recovery profiles are defined as the time from the end of anaesthesia to spontaneous respiration, adequate respiration, response to verbal command and extubation. The late recovery profiles are defined as achievement to Aldrete score of ten, post anaesthetic discharge score and psychomotor function evluation by Trieger Dot Test.

The secondary study objectives were to compare hemodynamic response to surgical and anaesthetic procedures, number of treated responses, number of fentanyl rescue for post-operative pain, adverse effects and other recovery profiles.

MATERIAL AND METHOD

The study was performed at two medical centers in Thailand after the protocol was approved by both institutional review boards, and written informed consent was obtained from all patients. The study consisted of 20 open labels followed by a double blind active parallel control group. One hundred and twenty six patients ranging in age from 18-65 years, ASA physical status I or II, scheduled for laparoscopic gynaecological procedures in an out-patient setting were selected as the double blind group. The expected operation time was less than 90 minutes. Patients were excluded if they had 1) 100 per cent or over ideal body weight 2) significant hypertension (diastolic blood pressure 100 mmHg or over) 3) malignant arrhythmia such as atrial fibrillation or supraventricular tachyarrhythmia 3) a chronic user of drugs that could cause abnormal psychomotor tests such as opioids, benzodiazepine and anti-convulsants 4) a history of opioid use and NSAID abnormal reaction including peptic irritation and 5) pregnant or lactating women. Pregnancy tests were checked on the study day. Baseline hematology and biochemistry were recorded in all patients. Treatment with Remifentanil or Alfentanil was assigned according to block balanced randomi-

zation sequence supplied in hidden entry envelopes to each center. The study nurse prepared the study drug in both bolus and infusion syringes labeled with the appropriate dose volume or rate of infusion based on the patient's weight. To maintain blinding of the study, the volume (ml) and rate of infusion (ml/h) were identical for both groups.

Pre-operative procedures included history taking and physical examination. Naproxen 500 mg was given orally with 30 ml clear fluid for post operative pain control at least 30 minutes before induction of anaesthesia. Intravenous catheters were placed and blood pressure at rest was checked twice at least 15 minutes apart between each reading. The lowest values of systolic, diastolic blood pressure and pulse rates were used as baseline control. In the operating theatre, all patients were monitored with electrocardiography using Lead II, automatic non-invasive blood pressure, pulse oximeter and capnometer. All parameters were recorded at the following time before induction, during induction, intubation, 1,3 and 5 minutes after intubation, incision, introduction of the laparoscope and every five minutes during the procedures. Every minute for the five minutes before the expected end of the procedure, at 1,3,5,7 and 10 minutes after the end of the procedure and study drugs had been stopped, then every 5 minutes until fully awake, extubation and discharge to the post anaesthetic care area.

Patients breathed 100 per cent oxygen, midazolam (1 mg) was given intravenously 3 minutes before induction with the bolus dose of study drugs, followed by propofol (2 mg/kg) and atracurium (0.5 mg/kg) to assist ventilation until full relaxation and tracheal intubation was performed. Controlled ventilation with O_2 and ventilator setting was adjusted to maintain end tidal carbon dioxide of 25-40 mmHg for the whole operation. Atracurium was added as needed for relaxation. Anaesthesia was maintained with the study drug and propofol 150 μg/kg/min until the introduction of the laparoscope. Then the infusion rate of propofol was reduced to 100 μg/kg/min. Before skin closure 0.25 per cent marcaine was infiltrated into the surgical wound. At the end of the operation, all infusions were stopped, atropine 1.2 mg and prostigmine 2.5 mg were used to reverse the neuromuscular blockade. Continuous evaluation of breathing, stage of conciousness and hemodynamic parameters which included end tidal carbon dioxide were done. The endotracheal tube was removed when the patient was clinically able to breathe adequately. Aldrete score was evaluated and recorded at 2,5,7,10 and 15 minutes and every five minutes until a score of 10 was achieved on two records. Time to spontaneous respiration, adequate respiration, response to verbal command to open eyes, ability to state name and birth date were recorded.

Remifentanil 1 μg/kg was used for bolus injection and a continuous infusion of 0.5 μg/kg/min was performed until the introduction of the laparoscope.Then the infusion rate was reduced to 0.25 μg/kg/min. Alfentanil 20 μg/kg was used for the bolus injection followed by a continuous infusion of 1 μg/kg/min which was later reduced to 0.5 μg/kg/min after the insertion of the laparoscope. If the systolic blood pressure was raised by more than 15 mmHg from the control value, heart rate more than 90 beats/minute and there was sweating or movement, then a bolus injection of 1 μg/kg of Remifentanil or 10 μ/kg of Alfentanil was given no more than two times while the infusion rate of Remifentanil 0.25 μg/kg/min or Alfentanil 0.5 μg/kg/min could be increased each time without exceding 2 μg/kg/min Remifentanil and 4 μg/kg/min for Alfentanil. If increasing the opioid was still unsuccessful to control responses to surgical stimuli, then propofol was added in a bolus of 10-20 mg, 1-2 times or propofol infusion was increased at a rate of 50 μg/kg/min at each increment.

If the systolic blood pressure decreased to below 80 mmHg, then the rate of intravenous fluid was increased and the propofol rate was decreased by 25 μg/kg/min each time but not lower than 75 μg/kg/min or decreased the rate of Remifentanil or Alfentanil infusion by 0.25 μg/kg/min and 0.5 μg/kg/min, respectively. The study drugs were not allowed to be lower than 0.125 μg/kg/min of Remifentanil or 0.25 μg/kg/min of Alfentanil .Atropine was given when the heart rate fell below 40-45 beat/min. or bradycardia was judget to be the cause of hypotensive response.

For the double blind, randomized part of the study, codes were prepared in closed envelops. The study nurse who was responsible for drug preparation opened and prepared the study drugs in concentration of either Remifentanil or Alfentanil in the syringe which could be calculated by

each subject's body weight. All syringes were labelled by subject number of bolus, infusion and supplement syringes. After handing the prepared syringes to the anaesthetic team, she was not in volved in the care of the subject in order to preserve the integrity of the blind study.

The occurrence of hemodynamic responses to tracheal intubation, surgical incision, introduction of trocha and surgical stimuli were recorded, as were any requirements of additional study drug boluses, increases in infusion rates, or propofol requirement. The number of patients requiring treatment for hypotension or bradycardia was also recorded.

During the recovery period, Aldrete score, modified post-anaesthetic discharge score that included bleeding, ability to sit, walk and the visual analogue pain score were evaluated every 15 minutes until they were ready to be discharged from the hospital. During the recovery phase, patients also completed the Trieger Dot test to evaluate their psychomotor function. These were performed 30 minutes before surgery (baseline) then 30, 60, and 90 minutes after termination of the study drugs. Pain was assessed by visual analogue pain scale every 15 minutes postextubation. If the visual analogue pain score was 2-3, fentanyl 12.5 μgm was given intravenously and if the score was more than 3, fentanyl 25 μgm was given. Pain score less than 2 was acceptable. Repeated dose was done if the pain score was not reduced to an acceptable level at 10 minute intervals.

All patient records were checked and evaluated in accordance with the Good Clinical Practice guideline. Recovery profile was analyzed by using an independent sample *t*-test, Wilcoxon rank sum test was used to analyse the Aldrete score and post-anaesthetic discharge scores. Comparative hemodynamic response during anaesthesia, and post operative rescue of fentanyl was analysed using the Mantel-Haenzel Chi square test. Psychomotor recovery was analysed comparing each individual scale by analysis of variance and all other hemodynamic parameters by independent *t*-test and Chi square test for adverse events. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 126 females entered the study. Four were withdrawn because of unexpected prolonged operations of more than 90 minutes in three patients and one who received 10 mg diazepam intravenously three hours before the procedure. Fifty-nine patients received Remifentanil and sixty-three received Alfentanil. The demographic data and baseline characteristics are shown in Table 1. The two treatment groups were well matched with respect to age, weight, ASA physical status, duration of anaesthesia and surgery.

Table 1. Demographic data, ASA physical status, average value expressed as mean ± SD (p value > 0.05 in all categories).

	Remifentanil	Alfentanil
No. of patient	59	63
Age	33.2 ± 5.5	34.0 ± 4.7
Weight	55.1 ± 8.6	53.9 ± 8.6
ASA physical status		
Class I	59	60
Class II	-	3
Duration of anaesthesia (min)	42.5 ± 17.4	38.4 ± 11.9
Duration of operation (min)	24.0 ± 17.7	20.2 ± 10.8

Duration of anaesthesia = time from induction to extubation
Duration of operation = time from skin incision to study drug discontinuation

The hemodynamic parameters are shown in Fig. 1. Patients receiving Remifentanil showed significantly fewer responses (hypertension, tachycardia, somatic or autonomic responses) to surgical stimuli (p value < 0.05) than those receiving Alfentanil (Table 2) and also required fewer additional boluses or adjustment in infusion rates of the study drugs and propofol (p value <0.05).

The incidence of hypotension was not different between the two groups. Most hypotensive episodes responded quickly with fluid load, except one patient from each group who needed ephedrine 6 mg intravenously to restore systolic blood pressure. Bradycardia occured significantly more often in the Remifentanil group (Table 2) which also needed more atropine 0.6 mg intravenously than the Alfentanil group (p value < 0.05).

Recovery time was similar for both Remifentanil and Alfentanil-treated patients. There was no significant difference in the time to respond to verbal commands between the two groups (Table 3). Time to spontaneous and adequate respiration and time to extubation were

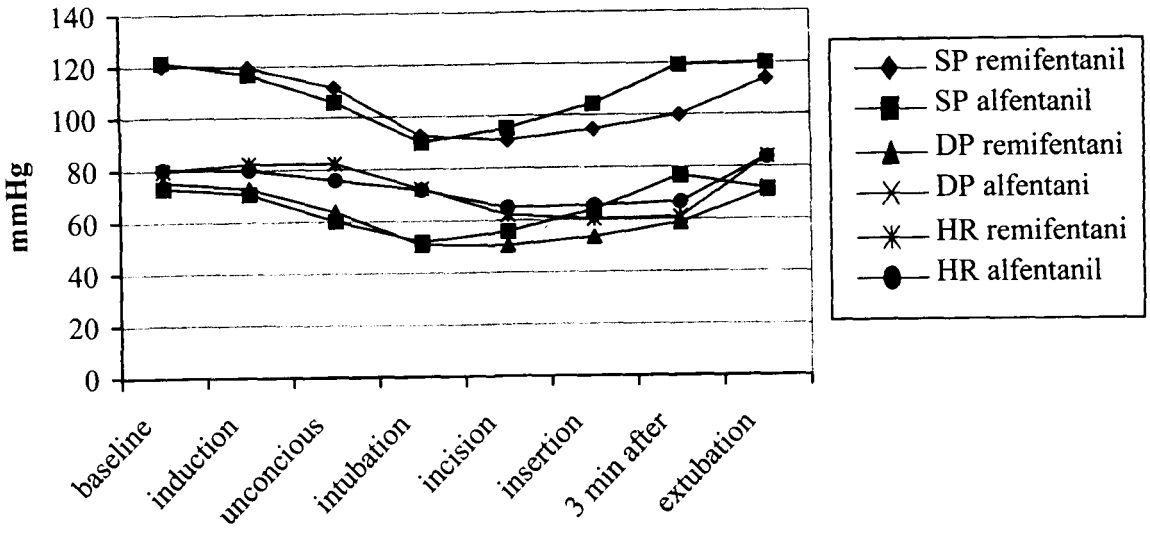

Fig. 1. Mean systolic pressure (SP), diastolic pressure (DP) and heart rate (HR).

Table 2. Number of hemodynamic response to surgical stimuli and number of infusion drag adjustment and atropine administration.

	Remifentanil (n=59)	Alfentanil (n=63)
Hypertension	2(3.4%)	18(28.6%)*
Hypotension	30(50.8%)	26(41.2%)
Bradycardia	14(23.7%)	5(7.9%)*
Drug incremental adjustment	1	17*
Drug decremental adjustment	14	7*
Atropine used for bradycardia	11	4*

* p value < 0.05

slightly lower in the Alfentanil group but the difference was not statistically significant.

The infusion rate of Remifentanil was reduced to 0.25 μgm/kg/min. before insertion of the laparoscope in 14 of 59 cases and the rate of 0.25 μgm/kg/min was used in 58 of 59 cases during the procedure. The infusion rate of Alfentanil was increased to 2.5 μgm/kg/min in three of 63 cases and all were reduced to 1.5 μgm/kg/min fifteen minutes after the beginning of the surgical procedure. The other eight cases needed 1 μgm/kg/min during maintenance period. In only 52 of 63 cases could the hemodynamic parameters be controlled by 0.5 μgm/kg/min. The average infusion dose of propofol was 86.5 μgm/kg/min in both groups.

Patients in the Remifentanil group recovered to a score of 10 Aldrete score slightly faster than the Alfentanil group and statistically significant at 50 and 60 minutes (p value < 0.05, Table 4) but they needed more fentanyl to control their post-operative pain within 60 minutes after operation than patients in the Alfentanil group (p value < 0.05, Table 5). Post-operative sedation score, post anaesthetic discharge score and recovery of psychomotor function by using Trieger Dot test were not significantly different between the two study groups (p value < 0.05, Table 6). Patients in the Remifentanil group had a significantly higher pain score and needed significantly more fentanyl at 30 and 60 minutes post operatively than the Alfentanil group (Table 5). Naproxen 500 mg orally before anaesthesia was not sufficient to control post-operative pain in this type of surgical procedure.

Post-operative incidence of nausea, emesis and urinary retention or postural hypotension were similar in both groups (Table 7). All patients were ready for discharge from the hospital within two hours post extubation except one patient in the Alfentanil group who needed five hours post-operative recovery because of urinary retention, nausea and severe emesis. Droperidol 2.5 mg

Table 3. Early recovery profile. mean (min)±SD, (range).

	Remifentanil	Alfentanil	p-value
Time to spontaneous respiration	5.2 ± 3.05 (1-14)	5.0 ± 2.49 (1-11)	0.615
Time to adequate respiration	8.4 ± 3.08 (3-18)	8.20 ± 3.09 (1-18)	0.721
Time to extubation	8.8 ± 3.05 (4-17)	8.7 ± 3.06 (2-18)	0.902
Time to response to verbal command			
Open eye	7.2 ± 2.86 (3-16)	7.5 ± 3.08 (2-16)	0.559
Lift limb	8.1 ± 2.65 (4-15)	8.2 ± 2.80 (3-16)	0.736
State name	9.3 ± 3.10 (5-18)	9.6 ± 3.12 (3-19)	0.782
State date of birth	9.7 ± 3.16 (5-18)	9.8 ± 3.19 (4-20)	0.890

Table 4. Percentage of patient who achieve Aldrete score 10 at time after stopping study drugs.

Time	Remifentanil (n=59)	Alfentanil (n=63)
5 min	8.5	3.2
10 min	49.2	49.2
20 min	78.0	77.8
30 min	91.5	81.0
40 min	94.9	85.7
50 min	100	90.5*
60 min	100	93.7*

* p value < 0.05

Table 5. Number of patient who require rescue fentanyl after stopping study drugs.

	Remifentanil	Alfentanil
Fitst 30 min	8	2*
30-60 min	26	9*
60-90 min	4	6
More than 90 min	2	5

* p value < 0.05

Table 6. Post-operative sedation score, Post-anaesthetic discharge score and Trieger Dot Test (mean score, p value > 0.05 in all categories).

	Sedation score		Postanaesthetic discharge score (PADS)		Trieger post test	
	Remifentani	Alfentanil	Remifentani	Alfentanil	Remifentani	Alfentanil
Preoperative	0.21	0.03	-	-	8.18	9.20
30 min Post-anesthetic time	3.01	2.46	8.93	9.08	21.01	21.83
60 min Post-anesthetic time	1.51	1.68	9.72	9.66	13.55	14.74
90 min Post-anesthetic time	0.77	0.86	9.91	9.87	10.93	10.58

Table 7. Post operation adverse events. (p value > 0.05 in all categories).

	Remifentanil	Alfentanil
Nausea	4	4
Emesis	1	2
Urinary retention	0	4

intravenously was used twice to treat emesis with partial success.

DISSCUSSION

Choosing the appropriate opioid for the ambulatory patient not only means effective blunting responses to intraoperative surgical stimuli, but a key to success which is based on rapid recovery, less nausea, vomiting and postural hypotension. Discharge criteria should include the ability to drink without vomiting, urination and adequate pain control. Giving opioids may prolong recovery time. Ideally, opioids for ambulatory anaesthesia should provide adequate analgesia to obtund response from surgical stimuli and provide rapid recovery with few postoperative side effects. Since Alfentanil is currently the short acting clinically available opioid, it was chosen as the reference drug to Remifentanil.

From this study we found little difference in recovery profile between the two opioids. Dose variation had an important effect on the result. The doses of Remifentanil in our study were derived from reviewing previous reports. The infusion dose of Remifentanil was approximately eight times more potent than Alfentanil[10-13]. For Alfentanil, many clinical studies[14-16] have recommended an Alfentanil bolus dose of 30 μg/kg alone or reduced one-third to one half in combination with propofol. Continuous infusion of Alfentanil has been studied by using target blood concentrations of three-compartmental pharmacological models but failed to maintain persistent correlation to analgesic level[15,17]. Without plasma concentration analysis, there are many ways to set up Alfentanil infusion such as double bolus with continuous infusion[18,19] or bolus together with propofol and continuous infusion starting from a very low dose as in this study which had to be changed several times before study state[12,13]. Patients receiving Alfentanil exhibited significantly higher responses to surgical stress and required more additional drugs than the Remifentanil group. We concluded that infusion dose of Alfentanil in this study was not enough to suppress surgical stimulation in this kind of operation. If the infusion dose of Alfentanil had been enough, it might have been possible to demonstrate significant difference in the recovery profiles of these two opioids.

There was a high incidence of intra-operative hypotension in both groups which usually happened a few minutes after intubation and before skin incision. This may be the vasodilating effect from both propofol and the study drug infusion. Though it could be easily treated with increasing fluid infusion rate, 200-300 ml of fluid load before induction of anaesthesia and reducing propofol infusion rate from 150 μg/kg/-min to 100 μg/kg/min after bolus dose may be helpful in reducing this incidence. Thai patients have demonstrated the need for lower doses of propofol infusion[20]. Bradycardia was the main side effect of Remifentanil and potentiated hypotensive response: A study by Song and White[21] found that the bolus dose of Remifentanil could be reduced to 0.5 μgm/kg with equally suppressed cardiovascular response to tracheal intubation in propofol induction.

Even though all the patients in this study had a rapid recovery profile with little difference between the two studied drugs, those in the Remifentanil group needed more post operative (30 - 60 minutes) analgesic supplement with fentanyl. This was due to the rapid wearing off of the ultra short acting Remifentanil. Oral administration of 500 mg Naproxen preoperatively was not effective for post-operative pain control in this study.

Step-wise intravenous fentanyl administration with respect to pain score was found to be effective in controlling postoperative pain without increasing the discharge time in this out-patient procedure. No significant difference was found in recovery and being ready to go home between these two opioids. The use of Remifentanil resulted in a better control of hemodynamic stress response to surgical stimuli but its ultrashort duration required more postoperative rescue analgesics.

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การศึกษาเปรียบเทียบระหว่างการใช้ Remifentanil หรือ Alfentanil ร่วมกับวิธีการ total intravenous anaesthesia ในการทำหัตถการโดยการส่องกล้องทางสูติ-นรีเวช สำหรับผู้ป่วยนอก

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คณะผู้ศึกษา ทำการศึกษาเปรียบเทียบการใช้ Remifentanil กับ Alfentanil เป็นยาระงับปวดร่วมกับการใช้ยา propofol ในวิธีการของ total intravenous anaesthesia และควบคุมการหย่อนตัวของกล้ามเนื้อด้วย atracurium เพื่อการส่องกล้อง ตรวจวินิจฉัยและทำหัตถการทางสูตินรีเวชในลักษณะการบริหารผู้ป่วยนอก โดยทำการศึกษาร่วมกันระหว่างภาควิชาวิสัญญีวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล และจุฬาลงกรณ์มหาวิทยาลัย ในรูปแบบ randomized, double blind ในผู้ป่วยจำนวน 126 คน ผู้ป่วย 59 คน ได้รับ Remifentanil และ 63 คน ได้รับ Alfentanil โดยมีผู้ป่วยถูกตัดออก 4 ราย จากระยะเวลาการผ่าตัดนานมากกว่า 90 นาที 3 ราย และผู้ป่วย 1 รายได้รับยา diazepan ก่อนการศึกษาการศึกษาครั้งนี้ใช้ Remifentanil 1 มคก./กก. บริหารเข้าทางหลอดเลือดดำและให้ต่อในขนาด 0.25-0.5 มคก./กก./นาที เปรียบเทียบกับ Alfentanil 20 มคก./กก. บริหารเข้าทางหลอดเลือดดำและให้ต่อในขนาด 0.5-1 มคก./กก./นาที ผลของการศึกษาพบว่า ผู้ป่วยกลุ่มที่ได้รับ Remifentanil แสดงการตอบสนองต่อการกระตุ้นระหว่างการทำหัตถการน้อยกว่ากลุ่ม Alfentanil อย่างมีนัยสำคัญทางสถิติ ($P < 0.05$) และกลุ่ม Alfentanil ต้องการยาเพิ่มเติมระหว่างการทำหัตถการมากกว่าอย่างมีนัยสำคัญทางสถิติ ($P < 0.05$) จากการศึกษานี้ไม่พบลักษณะการฟื้นตัวจากการสลบแตกต่างกันระหว่างยาทั้ง 2 ชนิด ไม่ว่าจะเป็นระยะเวลาที่ผู้ป่วยลืมตา ทำตามคำสั่ง หายใจได้เอง หรือการถอดท่อหายใจ ผู้ป่วยที่ได้รับ Remifentanil ต้องการยาระงับปวดในระยะหลังการผ่าตัดมากกว่า Alfentanil อย่างมีนัยสำคัญทางสถิติ ($P < 0.05$) จากการตรวจสอบ psycho-motor ของผู้ป่วยทั้ง 2 กลุ่มเปรียบเทียบกับก่อนได้รับยาพบว่า ที่เวลา 50 และ 60 นาที หลังจากหยุดยาผู้ป่วยกลุ่ม Remifentanil แสดงลักษณะการฟื้นตัวดีกว่า Alfentanil อย่างมีนัยสำคัญทางสถิติ พบอุบัติการณ์ของอัตราชีพจรที่ลดต่ำลงในกลุ่ม Remifentanil มากกว่า Alfentanil แต่ผลข้างเคียงอื่น ๆ รวมทั้งอาการ คลื่นไส้ อาเจียน ถ่ายปัสสาวะไม่ออกไม่แตกต่าง ผู้ป่วยทุกรายมีความ พร้อมที่จะเดินทางกลับจากโรงพยาบาลได้ภายในเวลา 120 นาที หลังจากถอดท่อช่วยหายใจ ยกเว้นผู้ป่วย 1 รายในกลุ่ม Alfentanil ที่ใช้เวลาอยู่ในโรงพยาบาลนาน 5 ชั่วโมง เนื่องจากถ่ายปัสสาวะไม่ออก คลื่นไส้ และอาเจียนอย่างมาก

คำสำคัญ : Ramifentanil, Total Intravenous Anesthesia, Out-Patient

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