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□ Clinical Research Article □

The hemodynamic changes during the infusion of remifentanil for patients under sevoflurane anesthesia during arthroscopic shoulder surgery

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Background: In spite of its minimal invasiveness, hemodynamic instability frequently happens during arthroscopic procedures. This study was performed to investigate the clinical efficacy of remifentanil for controlling the intra-operative hemodynamics during the performance of arthroscopic shoulder surgery.

Methods: Sixty patients (ASA class 1 and 2) who were scheduled for arthroscopic shoulder surgery were recruited for this study. After the induction and maintenance of anesthesia with thiopental sodium, rocuronium bromide, sevoflurane and nitrous oxide, the patients were randomly allocated to receive either saline or three different doses of remifentanil (0.03, 0.05 or 0.07 μg/kg/min) to assess the hemodynamic changes such as the systolic blood pressure, the diastolic blood pressure and the heart rate.

Results: The hemodynamics in the remifentanil groups were more stable than those in the saline group ($P < 0.05$), but there were some cardiovascular side effects such as hypertension (remifentanil 0.03 μg/kg/min), hypotension and bradycardia (remifentanil 0.07 μg/kg/min) with using remifentanil.

Conclusions: Remifentanil 0.05 μg/kg/min under anesthetic maintenance with sevoflurane showed better hemodynamic stability than the other two remifentanil groups during arthroscopic shoulder surgery. **(Korean J Anesthesiol 2009; 56: 497～501)**

Key Words: Arthroscopic surgery, Remifentanil, Shoulder.

INTRODUCTION

The frequency of arthroscopic surgery has been increasing because of its advantages such as small postoperative scar and fast recovery [1]. However, it may produce unstable hemodynamic changes caused by excessive pressure from irrigation fluid that is injected into the intra-articular space, its resultant extravasation [2], generalized absorption of epinephrine contained in the irrigation fluid and surgical nociceptive stress during arthroscopic shoulder surgery.

The remifentanil, as a new class of esterase metabolized opioid drug, has been frequently used to minimizing patient discomfort and hemodynamic changes throughout surgical procedures during anesthesia. In addition, regardless of exposure time, it has the least side effect due to quick onset time, short action duration and less accumulation effect than other opioids [3,4].

The authors wanted to identify the inhibitory effect of three different doses of remifentanil against the hemodynamic instability that occurs during arthroscopic shoulder surgery under general anesthesia using sevoflurane.

MATERIALS AND METHODS

This study enrolled 60 male and female patients (ASA class 1, 2) ranging from 20 to 70 who were going to have arthroscopic shoulder in the lateral decubitus position. We excluded those patients with cardiovascular disease, diabetes mellitus, neurovascular disease and thyroid disease, those with hemodynamic instability, and those who were taking medication that may affect blood pressure and heart rate. After getting approval from the hospital ethics committee, written informed consent was obtained from the patients and their families. All the

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subjects were randomly allocated to either group C (saline 20 ml/hr), group R1 (remifentanil 0.03 μg/kg/min), group R2 (remifentanil 0.05 μg/kg/min) or group R3 (remifentanil 0.07 μg/kg/min). There was no significant difference in age, gender, height, weight and ASA class (Table 1).

All the subjects were medicated (midazolam 0.05 mg/kg, im) 30 minutes before the induction of anesthesia. On arrival in the operating room, routine monitoring (electrocardiogram, peripheral pulse oximetry for oxygen saturation and noninvasive arterial pressure) was initiated. For continuous arterial pressure measurement the left radial artery was cannulated using 22 G catheter under topical anesthesia after carrying out modified Allen's test. Preoxygenation with 100% oxygen via face mask was started while infusing 10 ml/kg of lactated Ringer's solution before the induction of anesthesia. Anesthesia was induced with thiopental sodium 5 mg/kg and after loss of consciousness the patient's lungs were artificially ventilated with 100% oxygen. Neuromuscular blockade was provided with rocuronium bromide 0.9 mg/kg administered intravenously, the trachea was intubated later and controlled ventilation commenced. In all remifentanil patients respective infusion rate of remifentanil was maintained simultaneously. Anesthesia was maintained with oxygen (2 L/min), nitrous oxide (2 L/min) and sevoflurane (2 vol%, end-tidal concentration).

Measurements of systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and heart rate (HR) were taken when the patient was awake (Tbase) and at one minute before skin incision (Tb), 1 (T1), 5 (T5), 10 (T10), 15 (T15), 20 (T20) minutes after incision. Baseline awake values (Tbase) were recorded when vital signs were stabilized. Changes of more than 30% from the baseline values were considered significant and any changes about such respective factors defined as hypertension, hypotension bradycardia and tachycardia. If the SAP was above 165 mmHg or DAP above 95 mmHg, we injected nicardipine 15 μg/kg, and in cases where the SAP fell below 80 mmHg or mean arterial pressure (MAP) fell below 60 mmHg, ephedrine 5 mg or phenylephrine 50 μg was given. For a HR below 50 beats/min, we administered atropine 0.5 mg intravenously. The Frequency of hypertension, hypotension, bradycardia and tachycardia was also recorded.

Results were presented as mean ± standard deviation and statistical analysis was performed using statistical software packages (SPSS for windows, version 12.0, SPSS Inc, Chicago, USA). Sex and frequencies of hypertension, hypotension, tachycardia and bradycardia were analyzed with a chi-square test or Fisher's exact test, and age, weight and height were analyzed with the Mann-Whitney test. For the changes of blood pressure and heart rate in each group, we used repeated measures ANOVA and post-hoc Bonferroni test. For the inter-group comparison one way ANOVA with post-hoc Tukey HSD test was used. A value of $P < 0.05$ was considered statistically significant.

RESULTS

Before the induction of anesthesia, baseline SAP, DAP and HR were not significantly different among the groups (Fig. 1−3).

SAP significantly increased in group C at 5, 10, 15, and 20 minutes after incision in comparison to the baseline (Fig. 1). While group R1 and R2 did not show any significant change during the same period, SAP in group R3 decreased significantly at 20 minutes after incision. SAP in group R2 and R3 significantly decreased over the study period compared with group C.

DAP of group C significantly increased at 1, 5, 10, 15, and 20 minutes after surgical incision, but there was no significant changes in DAP for group R1, R2 and R3 in comparison to the baseline values but for group R3 at 20 minutes (Fig. 2). Changes between groups were most prominent in group R3 in comparison to group C.

Table 1. Demographic Data

	Group C (n = 15)	Group R1 (n = 15)	Group R2 (n = 15)	Group R3 (n = 15)
Sex (M/F)	9/6	8/7	7/8	7/8
Age (yr)	43.3 ± 15.4	44.4 ± 13.1	49.2 ± 14.1	42.7 ± 12.8
Weight (kg)	70.2 ± 8.8	63.7 ± 10.3	62.4 ± 8.7	60.7 ± 10.0
Height (cm)	170.2 ± 11.7	166.4 ± 8.2	163.2 ± 10.0	163.2 ± 9.2
ASA (1/2)	10/5	10/5	7/8	8/7

Values are mean ± SD. There were no significant differences among four groups. Group C: saline 20 ml/hr, Group R1: remifentanil 0.03 μg/kg/min, Group R2: remifentanil 0.05 μg/kg/min, Group R3: remifentanil 0.07 μg/kg/min.

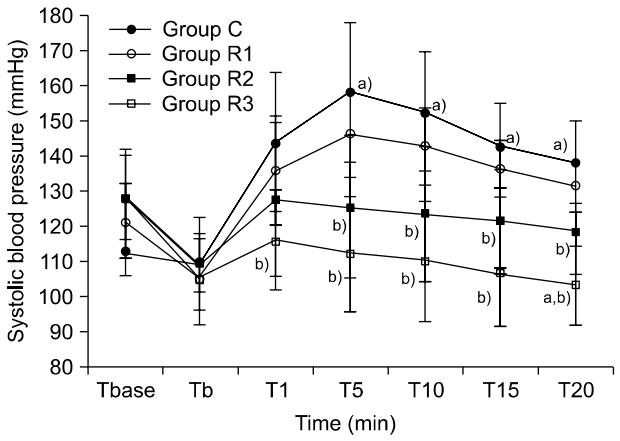

Fig. 1. Changes of systolic arterial pressure in four groups. Tbase: before anesthesia, Tb: 1 minute before incision, T1, T5, T10, T15 and T20: 1, 5, 10, 15 and 20 minutes after incision, respectively. Group C: saline 20 ml/hr, Group R1: remifentanil 0.03 μg/kg/min, Group R2: remifentanil 0.05 μg/kg/min, Group R3: remifentanil 0.07 μg/kg/min. Values are expressed as mean ± SD. $^{a)}P < 0.05$ compared with Tbase, $^{b)}P < 0.05$ compared with group C.

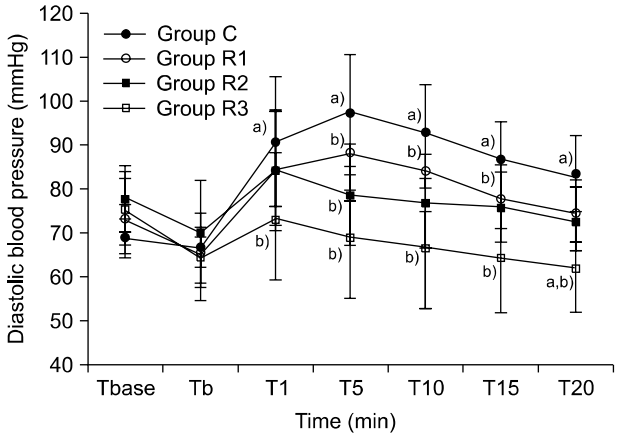

Fig. 2. Changes of diastolic arterial pressure among four groups. Tbase: before anesthesia, Tb: 1 minute before incision, T1, T5, T10, T15 and T20: 1, 5, 10, 15 and 20 minutes after incision, respectively. Group C: saline 20 ml/hr, Group R1: remifentanil 0.03 μg/kg/min, Group R2: remifentanil 0.05 μg/kg/min, Group R3: remifentanil 0.07 μg/kg/min. Values are expressed as mean ± SD. $^{a)}P < 0.05$ compared with Tbase, $^{b)}P < 0.05$ compared with group C.

HR also showed similar changes to SAP and DAP. HR of group C increased significantly at most of time points after incision in comparison to the baseline awake value (Fig. 3). HR of group R1, R2 and R3, however, did not change significantly. Inter-group changes were significant in group R2 and R3 compared with group C.

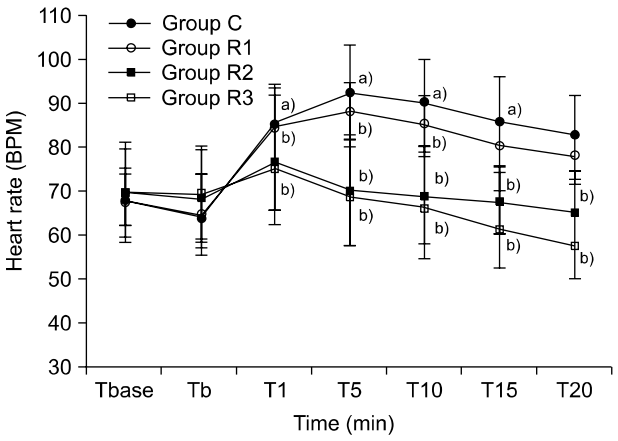

Fig. 3. Changes of heart rate among four groups. Tbase: before anesthesia, Tb: 1 minute before incision, T1, T5, T10, T15 and T20: 1, 5, 10, 15 and 20 minutes after incision, respectively. Group C: saline 20 ml/hr, Group R1: remifentanil 0.03 μg/kg/min, Group R2: remifentanil 0.05 μg/kg/min, Group R3: remifentanil 0.07 μg/kg/min. Values are expressed as mean ± SD. $^{a)}P < 0.05$ compared with Tbase, $^{b)}P < 0.05$ compared with group C.

Table 2. Incidence of Cardiovascular Side Effects

	Group C (n = 15)	Group R1 (n = 15)	Group R2 (n = 15)	Group R3 (n = 15)
Hypertension	11 (78.3%)$^{a)}$	5 (33.3%)	0 (0%)	0 (0%)
Tachycardia	4 (26.6%)$^{a)}$	0 (0%)	0 (0%)	0 (0%)
Hypotension	0 (0%)	0 (0%)	0 (0%)	3 (20.0%)
Bradycardia	0 (0%)	0 (0%)	0 (0%)	5 (33.3%)$^{a)}$

Values are number of patients (percent). Group C: saline 20 ml/hr, Group R1: remifentanil 0.03 μg/kg/min, Group R2: remifentanil 0.05 μg/kg/min, Group R3: remifentanil 0.07 μg/kg/min. $^{a)}P < 0.05$.

Hypertension and tachycardia were frequent in group C and some episodes of hypertension were observed in group R1. Hypotension and bradycardia occurred in group R3 (Table 2).

DISCUSSION

Compared with past classic method that shoulder joints are open for surgery, arthroscopic surgery has many advantages such as less scaring, infection and pain, shorter hospitalization and rapid recovery. Because of these, it has been extensively used for diagnosis and treatment of rotator cuff injury, joint dislocation, and supra-acromial space disease [1,5]. However, as the operation field of arthroscopic surgery is focal, visualization may be very poor when bleeding occurs. Efforts to overcome this problem have been tried and a few common

methods such as the use of epinephrine irrigation fluid for vasoconstriction and increased flow rate of irrigation fluid to eliminate blood and operative floaters have been usually used by many surgeons, but an unstable hemodynamic change like hypertension and tachycardia also had been accompanied by them. High concentration of inhalation agents [6], vasodilators such as sodium nitroprusside and nitroglycerin [7], a calcium channel blocker such as nicardipine [8,9], α and β receptor blockers [10], or an opioid had been used to mitigate the hemodynamic changes. However, such medications may cause complications such as reflex tachycardia, rebound hypertension, bradycardia, tachyphylaxis, myocardial depression, delayed awakening and respiratory depression [11]. In particular, opioids provide the hemodynamic stability and effective postoperative analgesia, but has much limitation of its use as they may be accompanied by postoperative respiratory depression, delayed awakening, intraoperative hypotension and bradycardia [12,23].

Remifentanil has been frequently used for controlling hemodynamic changes during total intravenous anesthesia (TIVA) and general anesthesia with inhalation agents as it has a quicker onset time, a shorter duration of action and a more rapid recovery than other opioids. Unlike other opioids metabolized by the liver and excreted through the kidneys, remifentanil is rapidly metabolized by non-specific tissue and plasma esterase extensively distributed in bodies regardless of exposure time. Therefore, the clearance of remifentanil is not affected by hepatic or renal dysfunction [13,14].

It's strong analgesic effect also provides stable hemodynamic profiles throughout the surgical procedure and especially, during induced hypotensive anesthesia, it maintains cerebral blood flow reaction without complication in the major organs [15].

Choi et al. reported that in the orthognathic two jaw surgeries, remifentanil 0.1 μg/kg/min while maintaining 1 MAC of sevoflurane's end-tidal concentration (ETSevo) resulted in the same induced hypotensive effect as nitroglycerin 1 μg/kg/min and rapid recovery time after discontinuation of drug infusion [16]. Degoute et al. reported that induced hypotensive anesthesia with 0.2−0.5 μg/kg/min remifentanil and about 2 vol% of ETSevo in middle ear surgery decreased by 25% of middle ear blood flow with stable hemodynamics , the good surgical filed rating and no complication [17]. Muñoz et al. suggested during TIVA with propofol for inguinal surgery, adults require about 0.08 μg/kg/min to block the somatic response to skin incisions [18]. Castanelli et al. reported that the mean MAC of sevoflurane was 2.39 ± 0.58 with remifentanil 0.03 μg/kg/min, 1.91 ± 0.36 with remifentanil 0.06 μg/kg/min, and 0.92 ± 0.11 with remifentanil 0.12 μg/kg/min [19]. Hwang et al. suggested that remifentanil 0.1 μg/kg/min for laparoscopic gynecologic surgery is effective in decreasing the concentration of sevoflurane while keeping hemodynamic stability [20]. Song and White also reported that the adjunctive use of remifentanil 0.07 ± 0.03 μg/kg/min during desflurane- N2O anesthesia facilitated early recovery without complication and hemodynamic instabilities [21]. As it has been known that arthroscopic shoulder surgery gives less pain than other operative methods but shows unstable hemodynamic changes during surgeries, we decided to provide remifentanil 0.03, 0.05, and 0.07 μg/kg/min with 2 vol% ETSevo to identify its adequate continuous infusion rate. The groups which received 0.03 μg/kg/min and 0.05 μg/kg/min remifentanil showed a slight increase in blood pressure, but relatively stable blood pressure was maintained, which was similar to the baseline awake value.

Remifentanil has side-effects like other opioids as mentioned above. As it has been reported that anesthesia for which high doses of opioids are used may cause rigidity of the chest wall, hypotension and bradycardia, much care should be taken [22]. In this study, remifentanil 0.07 μg/kg/min showed high frequencies of hypotension and bradycardia, but those side effects were not found in remifentanil at 0.05 μg/kg/min.

As there are no bibliographical data that present clear causes for hemodynamic changes during arthroscopic shoulder surgery, we assumed a few causes. First, it may be a response from the systemic absorption of epinephrine within the irrigation fluid. Except where excessive epinephrine mixed irrigation fluid was injected accidentally into bone marrow and caused severe hypertension [23], no cardiovascular adverse reactions were observed resulting from the intra-articular epinephrine administration [24]. We also assume that when systemic absorption of tiny amounts of epinephrine (1 : 1,000,000) added to irrigation fluid occurs, blood pressure decreases as more because β effects occur rather than α. Second, the numbers of incisions for manipulation may be a causative factor for unstable hemodynamics. However, we observed that the parts to be incised for the arthroscopic insertion were three at maximum, and blood pressure tended to gradually increase rather than decrease immediately after the incisions. We assume that the numbers of incisions don't contribute to increases in blood pressure. Third, according to the bibliographical data, it is effective to maintain a difference of less than 49 mmHg between systolic blood pressure and subacromial space pressure

(SASP) to decrease bleeding in capillary vessel for adequate visualization [2], and in case of poor operative field, surgeons ask increase of SASP, which may be causative of pain due to increased intra-articular fluid pressure and destruction of the surrounding tissue. This study did not identify the relevance of the causes as shoulder joint monitoring was not conducted.

In conclusion, we suggest that remifentanil 0.05 μg/kg/min with 2 vol% ETSevo for arthroscopic shoulder surgery is adequate infusion rate that minimizes side effect caused by opioid and hemodynamic changes caused by operative manipulation.

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