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ORIGINAL

A comparison of the hemodynamic responses between fentanyl and fentanyl-remifentanil in total intravenous anesthesia for orthognathic surgery

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ABSTRACT :

Background: The purpose of this retrospective study was to examine whether total intravenous anesthesia (TIVA) with fentanyl-remifentanil has potential hemodynamic advantages over that with fentanyl alone in orthognathic surgery.

Methods: The subjects were 42 generally healthy patients who underwent orthognathic surgery under TIVA using propofol and opioids. Nineteen patients received fentanyl alone
(F group), and 23 received fentanyl and remifentanil (FR group) as narcotic analgesics. The factors investigated included arterial blood pressure (ABP), heart rate, the lability index (L.I.) of ABP, number of case that required ephedrine and hypotensive anesthesia. The data between the two groups were compared using the Student's t-test or Fisher's exact test.

Results: The ABP during anesthesia was significantly lower in the FR group than in the F group. The L.I of the ABP in the FR group was significantly lower than in the F group. The total dose of nitroglycerin for hypotensive anesthesia in the FR group was significantly smaller than that in the F group. The number of cases that required ephedrine was significantly higher in the FR group than in the F group, but hypotension that required administration of ephedrine easily improved, and no refractory hypotension was observed.

Conclusion: Total intravenous anesthesia with fentanyl-remifentanil provides superior hemodynamic stability without unacceptable changes in the intraoperative ABP.

Key Words : Fentanyl; Remifentanil; Hemodynamic Stability; Total Intravenous Anesthesia; Orthognathic Surgery.

Introduction

Before approval of remifentanil in Japan, we usually used only fentanyl citrate (fentanyl) as a narcotic analgesic for general anesthesia. Although fentanyl is able to provide continuing analgesic effect postoperatively, it carries a risk of respiratory depression on the emergence and delayed emergence from anesthesia.

Remifentanil hydrochloride (remifentanil) has a rapid offset because of the short context-sensitive half-time[1]. Accordingly, we can administer remifentanil with little concern about respiratory depression on the emergence and delayed emergence from anesthesia. As a result, when using remifentanil, we can expect to block operative stimulation properly during surgery[2]. There are many comparative studies of fentanyl and remifentanil in general anesthesia[2−4]. However, to our knowledge, no comparative studies have been conducted for fentanyl and fentanyl-remifentanil as total intravenous anesthesia (TIVA) in the oral and maxillofacial region.

This retrospective study was conducted to clarify the

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hemodynamic advantages of management with different opioids in orthognathic surgery.

Methods

This study was approved by the Institutional Review Board of Hokkaido University Hospital (clinical study code 012-0202) and was carried out according to the principles of the Declaration of Helsinki and its amendments.

Patients

Study subjects were 42 patients (American Society of Anesthesiologists [ASA] physical status I or II) who underwent orthognathic surgery under TIVA using propofol and opioids at Hokkaido University Hospital from May 2006 to October 2008. The subjects were divided into two groups: those who received fentanyl alone (F group, n = 19) and those received fentanyl and remifentanil (FR group, n = 23) as narcotic analgesics. We excluded cases in which an arterial catheter was not inserted and continuous arterial blood pressure (ABP) was not measured as well as cases in which demographics records or operation/anesthesia management, hemodynamic or recovery data were incomplete.

Anesthetic methods

The measurement of electrocardiography (lead II), pulse oximetry, the noninvasive blood pressure (BP), the end-tidal carbon dioxide partial pressure and the bispectral index (BIS) were performed before the induction of anesthesia.

After preoxygenation with 100 % oxygen, anesthesia was induced with 2-4 μg/kg of intravenous fentanyl. Subsequently, propofol was administered through the Terufusion® target-controlled infusion (TCI) pump (TE-371; Terumo Corp., Tokyo, Japan), which used a Diprifusor® TCI system (Astra-Zeneca, London, UK). The initial propofol target concentration was set at 4.5-5.0 μg/ml. Intravenous (IV) vecuronium bromide or rocuronium bromide was administered to facilitate tracheal intubation.

Anesthesia was maintained by propofol infusion with a TCI pump under a fresh gas flow of oxygen and air mixture while monitoring the BIS (40-60). Before surgery, an arterial line was placed, and the invasive ABP was measured. In the operative field, 2 % lidocaine with 1/160,000 adrenaline was injected by a surgeon. The F group patients received a maintenance dose of intravenous fentanyl. Additional administration of fentanyl was given at the discretion of the dental anesthesiologists in charge. The FR group patients received a continuous infusion of remifentanil and fentanyl boluses. The dental anesthesiologists in charge decided on additional dose of fentanyl and infusion rate of remifentanil. Hypotensive anesthesia was performed according to the judgment of the dental anesthesiologists in charge in both groups. IV dexametazone sodium phosphate (8 mg), IV droperidol (2.5 mg) and IV metoclopramide hydrochloride (10 mg) were administered for the prevention of postoperative nausea and vomiting (PONV).

The dental anesthesiologists in charge determined the adjustment of the infusion rate of propofol and the timing of the final dose of fentanyl. In the FR group, gradual tapering of remifentanil was performed. IV flurbiprofen axetil (50 mg) was administered to achieve postanesthetic analgesia. After the end of the operation, artificial ventilation was performed with 100 % oxygen at a fresh gas flow of 6 l/min. Before extubation, reversal of muscle relaxants was performed if necessary.

Data

Hemodynamic data during anesthesia were extracted from anesthesia records. The intraoperative intra-arterial systolic and diastolic BP (ASBP and ADBP), highest ASBP, lability index (L.I.) of ASBP and mean arterial pressure (MAP) and intraoperative heart rate (HR) were included. The lability of ASBP of each case was assessed using the L.I. advocated by Reich et al.[5]. The high L.I. for MAP indicates significant instability of circulatory dynamics[6]. The extubation time was defined as the time from the end of the operation to extubation. The number of cases where ephedrine hydrochloride (ephedrine), atropine sulfate and nitroglycerin (NTG) were administered was counted. In addition, we investigated the total dose of NTG in cases where it was given.

Statistical analyses

The data of the F and FR groups were compared using the Student's t-test. The categorical data of the two groups were compared using Fisher's exact test. A p-value of <0.05 was considered significant.

Results

The demographic characteristics and ASA physical status are shown in Table 1. There were no significant differences between the two groups except for the mean age.

The hemodynamics data in the F group versus the FR group are shown in Table 2. During surgery, the ASBP and ADBP of the FR group were significantly lower than those of the F group ($P < 0.001$, respectively). The highest ASBP of the FR group was significantly lower than that of the F group ($P<0.001$) (Table 2). The L.I. of the ASBP and MAP in the FR group was significantly lower than that in the F group ($P<0.001$, respectively) (Table 2). The HR of the FR group was significantly lower than that of the F group ($P = 0.003$).

The extubation time was similar and generally rapid in both groups (Table 3). Blood loss was similar between the two groups (Table 3).

In the FR group, even if the BP decreased, ephedrine alone was sufficient to control it. Any further treatment was unnecessary for hypotension (Table 3). During surgery, hypotensive anesthesia was performed in 94.7 % of cases in the F group and 65.2 % of cases in the FR group, showing a significant difference between the two groups ($P = 0.027$). The total dose of NTG was lower in the FR group than in the F group ($P = 0.002$) (Table 3).

	F group (n = 19)	FR group (n = 23)	P-value	
Gender (male/female)	5/14	9/14	0.515	*
Age (year)	28.5	23.6	0.016	**
SD	6.18	6.1		
Weight (kg)	55.7	58.4	0.483	**
SD	9.5	13.7		
Height (cm)	162.7	165.1	0.349	**
SD	7.8	8.4		
Body mass index	21	21.3	0.777	**
SD	2.5	3.8		
ASA physical status (1/2)	17/2	20/3	1	*

Table 1. Demographic characteristics (n=42)

There were no significant differences between the two groups except for the mean age.

F group: fentanyl alone group, FR group: fentanyl and remifentanil group, ASA: American Society of Anaesthesiologists, *: Fisher's exact test, **: Student's t-test

	F group (n = 19)	FR group (n = 23)	P-value	
ASBP (mmHg)	108.5	95	< 0.01 (0.0006)	**
SD	13.2	7.5		
ADBP (mmHg)	60.9	48.2	< 0.01 (0.00001)	**
SD	8.9	4.8		
HR (bpm)	76	67.8	< 0.01 (0.003)	**
SD	7.8	8.7		
The highest ASBP	143.9	118.8	<0.01 (0.0003)	**
SD	24.9	14.7		
ASBP L.I.	0.0608	0.0402	<0.01 (0.0003)	**
SD	0.0173	0.0157		
MAP L.I.	0.0686	0.0479	<0.01 (0.0005)	**
SD	0.018	0.0168		

Table 2. Mean of hemodynamic values, the highest ASBP and lability index (n=42)

During surgery, the ASBP and ADBP of the FR group were significantly lower than those of the F group. The highest ASBP of the FR group was significantly lower than that of the F group. The lability of ASBP of each case was assessed using the L.I. advocated by Reich et al.[5]. The high L.I. for MAP indicates significant instability of circulatory dynamics[6]. The L.I. of the ASBP and MAP in the FR group was significantly lower than that in the F group. The HR of the FR group was significantly lower than that of the F group.

**: Student's t-test, ASBP: intra-arterial systolic blood pressure, ADBP: intra-arterial diastolic blood pressure, MAP: mean arterial pressure, HR: heart rate, L.I.: lability index.

	F group (n = 19)	FR group (n = 23)	P-value	
Operetion time (hours : mins)	4:24	4:35	0.746	**
SD	1:59	1:53		
Anesthesia time (hours : mins)	5:51	6:02	0.759	**
SD	1:57	1:55		
Extubation time (min)	13.9	14.3	0.843	**
SD	3.8	7		
Blood loss (ml)	374.7	301.5	0.357	**
SD	280.3	216		
Fentanyl mean total dose (μg/kg)	13.9	9.2	0.001	**
SD	4.6	3.8		
Remifentanil mean total dose (μg)		4160		
SD		1710		
Propofol mean total dose (mg)	2342.4	2225.3	0.636	**
SD	832.3	702.1		
Ephedrine use (+ / -)	2/17	16/7	0.0001	*
(%)	10.5	69.5		
Atropine use (+ / -)	2/17	1/22	0.581	*
(%)	10.5	4.3		
Hypotensive anesthesia (+ / -)	18/1	15/8	0.027	*
(%)	94.7	65.2		
NTG mean total dose (μg/kg)	241.5	88.5	0.002	**
SD	191.3	97.1		

Table 3. Characteristics of operation and anesthesia management (n=42)

The extubation time was similar and generally rapid in both groups. Blood loss was similar between the two groups. During surgery, hypotensive anesthesia was performed in 94.7 % of cases in the F group and 65.2 % of cases in the FR group, showing a significant difference between the two groups. The total dose of NTG was lower in the FR group than in the F group.

NTG : nitroglycerin, * : Fisher's exact test, ** : Student's t-test

Discussion

Remifentanil has rapid offset because of a short context sensitive half time. So we can administer remifentanil without any concern for respiratory depression on the emergence and delayed emergence from anesthesia. As a result, remifentanil offers an attenuation of the surgical

stress. On the other hand, it has been known to cause cardiovascular side effects during administration and post-operative side effects such as PONV and increased postoperative pain.

The L.I. of ASBP and MAP, ASBP, ADBP, HR and the highest ASBP in the FR group were significantly lower than those in the F group. These results suggest that remifentanil might suppress surgical stress and bring stability of circulatory dynamics. These results match past reports[2, 7, 8]. However, in the FR group, remifentanil increased frequency of hypotension. Although, the BP in the FR group was significantly lower than that in the F group, we could improve hypotension with ephedrine and did not experience refractory hypotension. These results suggested that significant BP reduction in the FR group might be well controllable and rarely lead to adverse events. Cardiovascular side effects of remifentanil include hypotension and bradycardia[9–11]. These side effects usually occur with overdose of remifentanil. On the other hand, continuous intravenous infusion of the low dose remifentanil may cause BP stability[12]. In this study, the infusion dose of remifentanil was approximately 0.25 μg/kg/min, and this dose would not cause sever hypotension usually.

Considering the cases of induced hypotension anesthesia, the total dose of NTG in the FR group was significantly smaller than that of the F group. These results suggest that the FR group requires less hypotensive anesthesia. It may be one of the advantages of the FR group in terms of reducing medical costs and simplifying anesthesia management methods.

Anesthesia recovery comparison between remifentanil and fentanyl had been studied[13]. Demet et al.[13] concluded that extubation time was found to be significantly longer in fentanyl group than in remifentanil group in a TCI of propofol anesthesia. In addition to rapid offset of remifentanil, the total dose of fentanyl was less in the FR group compared with the F group in this study. From these findings, we predicted that the extubation time in the FR group would be shorter than the F group. However there was no significant difference in extubation time between the F and FR group in this study. Two possible explanations for this result were as follows: 1) the dental anesthesiologists in charge might administer less fentanyl in latter half of surgery in the F group in consideration of delayed emergence. This might have led to inadequate fentanyl administration. 2) In the FR group, due to the combination of the two opioids, the characteristic of early awakening of remifentanil was less notable.

Remifentanil-related side effects have been recognized. During administration of remifentanil, we need to be careful that remifentanil has cardiovascular side effects (such as hypotension and bradycardia). In this study, we investigated cardiovascular side effects (hypotension and bradycardia). Although, the BP and HR in the FR group was significantly lower than those in the F group, we could improve hypotension with ephedrine and did not need to provide treatment for bradycardia. On the other hand, in the FR group, there was an advantage of circulatory dynamics stability. Our findings suggest that remifentanil could be effective narcotic anesthetic for orthognathic surgery by monitoring circulatory inhibition carefully.

Several limitations associated with the present study warrant mention. First, we excluded some cases with inadequate data. Therefore, we had a small sample size. Second, the details regarding the method of anesthesia (e.g. use of NTG, administration of fentanyl and continuous infusion rate of remifentanil) were determined by the dental anesthesiologist in charge.

Conclusion

Total intravenous anesthesia with fentanyl-remifentanil provides superior hemodynamic stability without unacceptable changes in the intraoperative ABP.

Conflicts of interest: There are no conflicts of interest to declare.

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