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Effects of fentanyl on cardiovascular response during rapid sequence induction in hypertensive patients

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Abstract: This study was carried out to evaluate the effects of fentanyl on cardiovascular and catecholamine responses during rapid sequence induction (RSI) in hypertensive patients. Twenty-eight patients were allocated into one of 3 groups: group 1 ($n = 7$) consisted of normotensive patients receiving no fentanyl, group 2 ($n = 10$) consisted of normotensive patients receiving fentanyl, and group 3 ($n = 11$) consisted of hypertensive patients receiving fentanyl. RSI was performed with thiamylal (4 mg·kg^{-1}) and succinylcholine (2 mg·kg^{-1}) for all groups. In groups 2 and 3, fentanyl (4 μg·kg^{-1}) was given prior to induction. Measurements including systolic arterial pressure (SAP) and heart rate (HR) were made at preinduction (T1), preintubation (T2), 1 min after intubation (T3), and 3 min after intubation (T4). Simultaneously, plasma concentrations of epinephrine (E) and norepinephrine (NE) were measured at T1 and T3. Group 1 showed significant increases in SAP, HR, and NE at T3 as compared to T1. Group 2 showed a significant increase in HR at T3 but not in SAP or catecholamines. Group 3 showed no increase in SAP, HR, or catecholamines throughout the time course. The results suggest that fentanyl is useful to suppress sympathoadrenal and cardiovascular responses to RSI in hypertensive patients as well as normotensive patients.

Key words: Hypertension, Rapid Sequence Induction, Fentanyl, Catecholamine

Introduction

Rapid sequence induction (RSI) is a useful technique to prevent fatal complications including regurgitation, aspiration, and pneumonitis in patients with a full stomach [1–2]. However, RSI may cause increases in blood pressure and heart rate [3] resulting in myocardial ischemia or stroke. Several methods were evaluated in normotensive patients to reduce the hemodynamic changes or sympathoadrenal response produced by RSI [4–7]. Fentanyl was reported to be effective for stabilization of cardiovascular response to RSI in patients without hypertension [8], whereas no definite evaluation has been made in hypertensive patients. The present study was carried out to evaluate the effects of fentanyl on the cardiovascular response and plasma catecholamines during RSI in patients with treated hypertension.

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Materials and methods

The protocol was approved by the Human Research Ethics Committe of Nagasaki Rosai Hospital. Informed consent was obtained from all patients.

The subjects of the study were 28 ASA I or II patients undergoing elective orthopedic surgery, and they were allocated into one of three groups (Table 1). Group 1 consisted of 7 normotensive patients who received no fentanyl for anesthetic induction. Group 2 consisted of 10 normotensive patients who received fentanyl for anesthetic induction. Group 3 consisted of 11 hypertensive patients who received fentanyl for anesthetic induction. All of the hypertensive patients were treated preoperatively with antihypertensive drugs (nicardipine 20–60 mg·day^{-1}) to maintain systolic blood pressure under 160 mmHg.

The patients were premedicated with atropine (0.01 mg·kg^{-1}) and hydroxyzine (1 mg·kg^{-1}) intramuscularly, 30 min before the induction of anesthesia. The radial artery was cannulated under local anesthesia for direct blood pressure measurement and blood sampling. Heart rate was measured, and ST-T change and arrhythmias were observed with lead II ECG monitoring. Rapid sequence induction was conducted as follows. The patients were given vecuronium (15 μg·kg^{-1})

Table 1. Patient characteristics

	Group 1	Group 2	Group 3
Sex (M/F)	5/2	8/2	6/5
Age (year)	61.0 ± 3.3	60.6 ± 3.0	65.0 ± 3.4
Weight (kg)	59.9 ± 3.0	60.6 ± 2.1	55.0 ± 2.7
Int. time (s)	25.1 ± 1.5	25.3 ± 2.8	24.4 ± 5.2
SAP (mmHg)	138.6 ± 6.3	144.3 ± 5.0	164.8 ± 8.0
HR (bpm)	74.9 ± 5.2	75.2 ± 5.5	95.6 ± 6.9

Int. time, intubation time; SAP, systolic arterial pressure; HR, heart rate.
Values are expressed as mean ± SE.

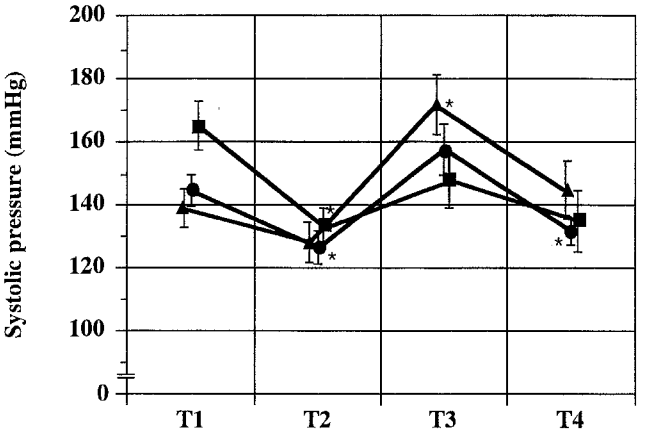

Fig. 1. Changes in systolic arterial pressure at preinduction (*T1*), preintubation (*T2*), 1 min after intubation (*T3*), and 3 min after intubation (*T4*) in normotensive patients without fentanyl (*triangles*, group 1), normotensive patients with fentanyl (*circles*, group 2), and hypertensive patients with fentanyl (*squares*, group 3). $^*P < 0.05$ compared to T1

iv for precurarization followed by 3-min inhalation of 100% oxygen. The patients in groups 2 and 3 received fentanyl ($4\,\mu g \cdot kg^{-1}$) iv, prior to vecuronium. Anesthesia was induced with thiamylal ($4\,mg \cdot kg^{-1}$) and succinylcholine chloride (SCC) ($2\,mg \cdot kg^{-1}$). Thiamylal was injected at a rate of $25\,mg \cdot s^{-1}$. Tracheal intubation was performed 1 min after the injection of SCC. Then, the patients were ventilated by 100% O_2 for 1 min followed by 67% N_2O and 1.5% sevoflurane.

Systolic arterial pressure (SAP) and heart rate (HR) were measured at preinduction (T1), preintubation (T2), 1 min after intubation (T3), and 3 min after intubation (T4). Blood samples were obtained from the radial arterial catheter at T1 and T3. All samples were taken into ice-cold plastic tubes containing ethylenediaminetetraacetate (EDTA) and centrifuged at 4°C. Plasma was stored at −40°C until analyzed for plasma concentrations of epinephrine (E) and norepinephrine (NE). E and NE in plasma were determined by high-performance liquid chromatography with UV detection [9]. This assay method has a limit of sensitivity of 40 pg for each catecholamine.

All values were expressed as mean ± SE. Differences were assessed with the Mann-Whitney U test or Wilcoxon signed-rank test. A P value less than 0.05 was considered significant.

Results

Table 1 shows the average age, weight, intubation time, SAP, and HR at preinduction.

Ischemic ECG changes such as ST-T changes or arrhythmias during induction were not observed on the monitor in any case.

Figure 1 shows SAP changes during anesthetic induction and tracheal intubation. Group 1 showed the baseline SAP of 139 ± 6 mmHg at T1, and a significant increase in SAP (172 ± 9) at postintubation (T3). Group 2 had a baseline SAP of 144 ± 5 and showed a significant decrease (126 ± 5) after induction (T2), but showed no significant increase (157 ± 8) at postintubation (T3). The SAP change in group 3 was similar to that in group 2, i.e., the baseline SAP of 165 ± 8 showed a significant decrease (132 ± 6) after induction (T2), but showed no significant increase (148 ± 9) at postintubation (T3). The percent change of SAP at T3 compared to T1 was +23.8% in group 1, +9.1% in group 2, and −10.4% in group 3, respectively. Figure 2 shows HR changes during anesthetic induction and tracheal intubation. Group 1 had a baseline HR of 75 ± 5 bpm at T1, and showed a significant increase at postintubation (94 ± 3). Group 2 had a baseline HR

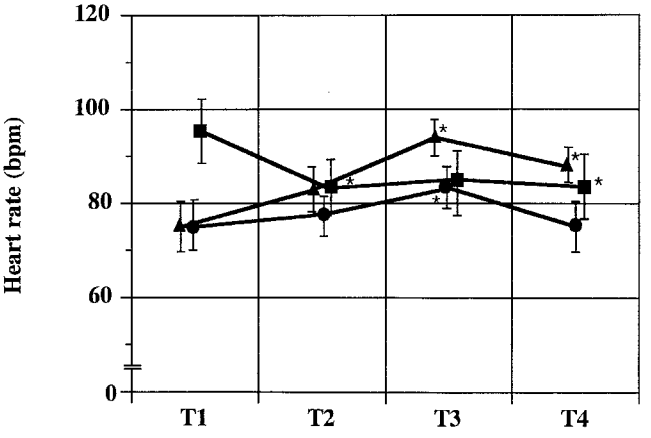

Fig. 2. Changes in heart rate at preinduction (*T1*), preintubation (*T2*), 1 min after intubation (*T3*), and 3 min after intubation (*T4*) in normotensive patients without fentanyl (*triangles*, group 1), normotensive patients with fentanyl (*circles*, group 2), and hypertensive patients with fentanyl (*squares*, group 3). $^*P < 0.05$ compared to T1

Table 2. Plasma catecholamine concentrations

	Epinephrine ($pg \cdot ml^{-1}$)		Norepinephrine ($pg \cdot ml^{-1}$)	
	T1	T3	T1	T3
Group 1 ($n = 7$)	40 ± 7	38 ± 14	180 ± 49	490 ± 75*
Group 2 ($n = 10$)	111 ± 28	67 ± 14	286 ± 34	320 ± 43
Group 3 ($n = 11$)	103 ± 14	56 ± 15*	460 ± 102	459 ± 95

T1, preinduction; T3, 1 min after intubation.
Values are expressed as mean ± SE.
* $P < 0.05$ *vs* T1.

of 75 ± 6, and showed a significant increase at postintubation (83 ± 5). Group 3 had a baseline HR of 96 ± 7, and showed no significant increase at postintubation (85 ± 7). The percent change of HR at T3 compared to T1 was +25.6% in group 1, +10.5% in group 2, and −11.2% in group 3.

Table 2 shows the plasma catecholamine concentrations at preinduction (T1) and 1 min after intubation (T3). Group 1 showed a significant increase in NE at T3 compared to T1, whereas neither group 2 nor group 3 showed a significant change in plasma NE. Group 3 showed a significant decrease in E at T3 compared to T1, whereas neither group 1 nor group 2 showed a significant change in plasma E. There was no significant difference between groups 2 and 3 in plasma E or NE throughout the time course.

Discussion

Certain techniques have been reported to reduce the unfavorable responses to laryngoscopy and tracheal intubation during RSI in normotensive patients. Randall et al. [4] reported that low-dose ($5 \mu g \cdot kg^{-1}$) fentanyl given during preoxygenation diminished the stress response to RSI in normotensive patients. Tomiyasu et al. [8] reported that supplementary doses of midazolam could reduce circulatory responses to induction of anesthesia and tracheal intubation in normotensive patients.

It has been reported that patients with essential hypertension have increased activity of the sympathetic nervous system [10–12], and show an exaggerated hemodynamic response to the induction of anesthesia compared to normotensive patients [13]. Thus, RSI is not recommended for patients with hypertension, because of the risk of hypertensive response. Chraemmer et al. [3] showed that both elective induction and RSI produced equal depression of left ventricular ejection fraction, but pronounced hypertension and tachycardia were observed during RSI. They also reported that higher myocardial oxygen consumption during RSI might represent a serious additional burden for the poorly perfused heart.

In the present study, we examined systolic arterial pressure and heart rate as parameters of hemodynamic change during RSI. The results show that fentanyl suppressed the hemodynamic response in hypertensive patients as well as normotensive patients. Rate pressure products were higher in hypertensive patients before induction of anesthesia (15840 ± 1438), but decreased to a similar level to that of normotensive patients after induction (10991 ± 798) and stayed within the normal range after intubation (12847 ± 1471). Hypertensive patients have an increased incidence of coronary arteriosclerosis and an increased risk of myocardial ischemia during induction. Thus, the present results are clinically significant especially in hypertensive patients.

Many authors have reported the plasma catecholamine concentrations in patients with essential hypertension. Goldstein [14] reviewed 78 reports on plasma catecholamines in patients with essential hypertension. He found that although most reports showed higher catecholamine levels in the hypertensives, only about 40% of the studies reported statistically significant differences. Kjeldsen et al. [15] reported that plasma E and NE were positively and significantly correlated with blood pressure in middle-aged men with untreated sustained essential hypertension. Some reports showed catecholamine levels during induction of anesthesia, especially after laryngoscopy in patients with hypertension. Low et al. [13] reported that there was a marked increase in NE concentration and a moderate increase in E concentration after laryngoscopy in hypertensive patients. Takino et al. [16] studied the effect of midazolam during induction in hypertensive patients and showed that catecholamine concentrations did not increase 1 min after intubation, and that E decreased significantly 3 min after intubation. In the present study, there was no difference in the E or NE concentration before induction between hypertensive and normotensive patients. The plasma concentration of E in the hypertensive patients significantly decreased after intubation, but the plasma concentration of NE showed no significant change. The results suggest that fentanyl suppresses sympathoadrenal response to tracheal intubation in hypertensive as well as normotensive patients.

We conclude that low-dose fentanyl is useful in inhibiting the hemodynamic and catecholamine responses to RSI in hypertensive as well as normotensive patients.

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