Single-Dose Intravenous Flurbiprofen Administration Increases Blood Pressure Under General Anesthesia In Normotensive Patients

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Citation

T Higashizawa, T Terai, M Yabe, T Yamashita, Y Hosono, K Ikeda, T Fuji, K Yoshimoto. *Single-Dose Intravenous Flurbiprofen Administration Increases Blood Pressure Under General Anesthesia In Normotensive Patients*. The Internet Journal of Anesthesiology. 2006 Volume 13 Number 1.

Abstract

We studied whether blood pressure elevation is influenced by intravenous single-dose administration of flurbiprofen during general anesthesia. Twenty female patients who underwent lower abdominal laparotomy under general anesthesia were divided into two groups. Both groups received anesthesia with nitrous dioxide, sevoflurane, and pentazocine. The flurbiprofen group (n=10) received 50 mg flurbiprofen intravenously 10 minutes after the start of the surgery. The control group (n=10) received 50 mg flurbiprofen at the end of the examination. Blood pressure was assessed before administration (0 minute as baseline) and after administration (15, 30 and 60 minutes). Systolic blood pressures inceased after 60 minutes in the flurbiprofen group (fluctuation ratio from baseline: 1.28±0.06, mean±SEM) compared with that in the control group (1.07±0.04, $p < 0.05$) and with baseline at 15, 30, and 60 minutes (1.17±0.05, 1.17±0.05, and 1.28±0.06, respectively, $p < 0.05$).

INTRODUCTION

Nonsteroidal anti-inflammatory drugs (NSAIDs), which are common analgesics, are very popular in all medical fields except pediatrics. In surgery, NSAIDs, rather than opioids, are standard analgesics. Although NSAIDs are efficacious, safe and easy, to use as potoperative analgesics, they are not appropriate for patients with severe hypertension, because NSAIDs often cause blood pressure to increase[1]. Some patients with no history of hypertension require treatment for hypertension when they receive of NSAIDs[2]. In reported cases, NSAIDs were administered for more than 1 month. However, NSAIDs have not been reported to cause changes in blood pressure when administered as a single-dose intraoperatively with general anesthesia, even in normotensive patients. Therefore, we examined the effects on blood pressure of administration of the NSAIDs flurbiprofen during general anesthesia in normotensive patients.

SUBJECTS AND METHODS

The subjects were 20 female patients with an American Society of Anesthesiologisits (ASA) physical status class I who underwent gynecological surgery. None of the subjects had circulatory complications. All patients had myoma uteri or ovarian cyst and were scheduled to undergo abdominal hysterectomy or removal of the ovarian cyst. This protocol was approved by the Ethics Committee of Osaka Rosai Hospital. All patients gave informed consent before participating in the study. Patients were randomly assigned to one of two groups according to a simple randomization table: a flurbiprofen group (n=10) and a control group (n=10). In each group, 7 patients underwent hysterectomy and 3 underwent ovarian cyst removal. General anesthesia was induced with 2 $mg*kg^{-1}$ propofol administered intravenously, and an endotracheal tube was inserted under muscle relaxation with 0.1 $mg*kg^{-1}$ vecuronium. General anesthesia was maintained with 0.5% to 5.0% sevoflurane in 67% nitrous dioxide in oxygen with a fresh gas flow rate of 3 $l*min^{-1}$. Five minutes before surgery, 15 mg of pentazocine was administered intravenously in each group for analgesia. Fifty milligrams of flurbiprofen was administered intravenously under general anesthesia 10 minutes after the start of the surgery which was the baseline in the flurbiprofen group and administered under general anesthesia at the end of the examination in the control group. Neither the anesthesiologists nor the surgeons were informed

when flurbiprofen was given. Systolic blood pressure was maintained until administration of flurbiprofen within 10% of the value when the patient was admitted to the operating room. General anesthesia was optionally maintained by the anesthesiologist to allow surgery to continue safely. All patients were admitted to the recovery unit for 30 minutes after surgery. When the absence of significant postanesthetic complications was confirmed, the patients were returned to their ward. Blood pressure, heart rate, SpO_2, $EtCO_2$, and the inspiratory sevoflurane concentration were evaluated 0, 15, 30, and 60 minutes after administration of flurbiprofen, and fluctuation ratios were calculated values and compared with the baseline which was the point of 0 minute and was the value 1.00.

DATA ANALYSIS

Data values expressed as means ±SD for background of patients and baseline and means ±SEM for fluctuation ratios from baseline. The results were analyzed for statistical significance using one-way analysis of variance (ANOVA), and the Mann-Whitney U-test was used to compare the background of patient. The unpaired Student's t-test was used to compare the data between two groups and the paired Student's t-test was used to compare the data of each group. The unpaired Student's t-test was also used to compare the data between the control group and the flurbiprofen group. Differences were considered significant at $p < 0.05$. For these analyses, we used Statview (version 5.0).

RESULT

The background of the patients did not significantly differ between the groups (Table 1), and there were no significant differences within each group at baseline (Table 2).

Figure 1

Table 1: Background of patients

Characteristic	control group (n = 10)	flurbiprofen group (n = 10)	*p*
Age (yr)	43 ±10	45±10	ns
Height (cm)	157 ±5	157±5	ns
Weight (kg)	51 ±9	50 ±8	ns
Body mass index ($kg.m^{-2}$)	20.8 ±4.3	20.3 ±3.3	ns
Blood pressure systolic	118 ±17	116 ±13	ns
(at admission, mmHg) mean	89 ±13	85 ±13	ns
diastolic	75 ±12	70 ±13	ns
Anesthesia time (min)	166 ±64	143 ±39	ns
Surgery time (min)	123 ±19	108 ±11	ns
Fluid intake ($ml.kg^{-1}.h^{-1}$)	11.3 ±3.4	13.3 ±4.5	ns
Urine output ($ml.kg^{-1}.h^{-1}$)	0.9 ±0.5	0.9 ±0.8	ns
Blood loss (g)	184 ±199	154 ±150	ns

Values are means ±SD.

Figure 2

Table 2: Time course fluctuation ratios from baseline of blood pressure, heart rate, SpO, EtCO, and sevoflurane concentration after administration of flurbiprofen

Characteristic	baseline	fluctuation ratio from baseline 15 (min)	30 (min)	60 (min)
		control group		
		flurbiprofen group		
Blood pressure (mmHg)				
systolic	118 ±17	0.97 ±0.03	1.06 ±0.03	1.07 ±0.04
	117 ±13	1.17 ±0.05*#	1.17 ±0.05*#	1.28 ±0.06*#
mean	82 ±10	0.97 ±0.03	1.04 ±0.03	1.05 ±0.03
	79 ±13	1.13 ±0.01	1.13 ±0.07	1.21 ±0.09#
diastolic	68 ±9	0.98 ±0.04	1.03 ±0.04	1.03 ±0.03
	65 ±14	1.02 ±0.04	1.14 ±0.11	1.16 ±0.11
Heart rate (bpm)	68 ±10	0.99 ±0.03	0.98 ±0.04	1.01 ±0.04
	63 ±7	1.04 ±0.02	1.03 ±0.04	1.00 ±0.04
SpO_2 (%)	98 ±1	1.00 ±0.02	1.00 ±0.03	1.00 ±0.02
	98 ±1	1.00 ±0.01	1.00 ±0.03	1.00 ±0.02
$EtCO_2$ (mmHg)	34 ±3	1.02 ±0.02	1.02 ±0.02	1.00 ±0.02
	33 ±2	1.00 ±0.01	0.98 ±0.01	0.96 ±0.01
Sevoflurane concentration (%)	2.0 ±0.8	0.84 ±0.07#	0.80 ±0.09	0.83 ±0.12
	2.1 ±0.3	0.95 ±0.05	0.88 ±0.08	0.85 ±0.09

Values are means ±SD at baseline and means ±SEM for fluctuation ratios. *: significant difference from control group ($p< 0.05$) # : significant difference from baseline ($p< 0.05$)

Systolic blood pressure in the flurbiprofen group at 60 minutes was significantly higher than that in the control group (Table 2). Mean and diastolic blood pressures at 15, 30, and 60 minutes did not differ significantly between two groups (Table 2). In the flurbiprofen group, systolic blood pressure at 15, 30, and 60 minutes and mean blood pressure at 60 minutes were significantly higher than at baseline (Table 2). In the control group, blood pressure at 15, 30, and 60 minutes did not differ significantly from that at baseline (Table 2). The inspiratory sevoflurane concentration did not differ significantly between the groups at 15, 30, and 60 minutes (Table 2) but at 15 minutes was significantly lower than at baseline in the control group (Table 2). Heart rate, SpO_2, and $EtCO_2$ were stable throughout this examination (Table 2).

DISCUSSION

Preoperative administration of NSAIDs for postoperative analgesia is often practiced under general anesthesia [3]. We occasionally encounter mildly hypertensive patients or normotensive patients who require treatment for hypertension during general anesthesia after administration of NSAIDs. In the present, blood pressure increased during surgery under general anesthesia when flurbiprofen was administered. Several previous studies have shown increase in systolic blood pressure [2,4]. Systolic blood pressure also changed markedly, and might even be why anesthesiologists monitor mainly the systolic blood pressure level during general anesthesia. Although blood pressure increased after administration of flurbiprofen, the heart rate and the inspiratory sevoflurane concentration did not change, indicating the effect of flurbiprofen administration rather than the effect of noxious surgical stimuli. Use of NSAIDs is contraindicated for patients with moderate to severe hypertension because NSAIDs increases blood pressure due to depression of the activities of prostaglandin E_2 and I_2 through inhibition of cyclooxygenase in renal arterioles[5,6]. In addition, systemic vasoconstriction may be effected endothelin-1 by NSAIDs [7]. Therefore, special careful must be taken when NSAIDs are administered to patients undergoing surgery and even when used to treat patients with pain or fever. The degree of blood pressure elevation seems to differ with the type of NSAIDs [8], and no previous studies have shown that flurbiprofen increases blood pressure. In the present, intravenously administered flurbiprofen increased blood pressure in normotensive patients, although not to a degree requiring treatment. Flurbiprofen is an NSAIDs that can be administered intravenously. As we often administer flurbiprofen during surgery to treat postoperative pain, care must be exercised, even in normotensive patients.

In conclusion, intravenous administration of flurbiprofen as a 50 mg single-dose to normotensive patients undergoing gynecological laparotomy increases blood pressure under general anesthesia.

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