

ORIGINAL ARTICLE

Randomized controlled trial to compare the effects of nicardipine and prostaglandin E₁ induced hypotension on arterial oxygen pressure in patients undergoing brain tumor resection under general anesthesia

Tomoki Nishiyama, MD, PhD

Department of Anesthesiology, Shinagawa Shishokai Hospital, 1-29-7, Kita-Shinagawa, Shinagawa-ku, Tokyo, 140-0001 (Japan)

Correspondence: Tomoki Nishiyama, MD, PhD, Department of Anesthesiology, Shinagawa Shishokai Hospital, 1-29-7, Kita-Shinagawa, Shinagawa-ku, Tokyo, 140-0001 (Japan); Tel: +81-3-5781-0700; Fax: +81-3-5781-0828; E-mail: nishit-ky@umin.ac.jp

ABSTRACT

Objective: Arterial oxygen pressure (PaO₂) may decrease at induced hypotension during general anesthesia by nicardipine or prostaglandin E₁ (PG). The present study was performed to compare the effects of nicardipine and PG on PaO₂ during induced hypotension in general anesthesia.

Methodology: This randomized controlled non-blind study was conducted at our operating room at the University Hospital.

Fifty patients aged 40 to 65 years for resection of brain tumor were enrolled in the study. During general anesthesia with isoflurane, nitrous oxide and fentanyl, when hemodynamics were stable, PG 0.05 μg/kg/min, or 0.1 μg/kg/min, or nicardipine 0.5 μg/kg/min, or 1.0 μg/kg/min was administered for two hours in 10 patients each. Another 10 patients were reserved as the control.

Arterial blood pressure, heart rate, percutaneous oxygen saturation (SpO₂), end-tidal carbon dioxide pressure (EtCO₂), and arterial oxygen (PaO₂) and carbon dioxide (PaCO₂) pressures were measured until 90 min after stop of administration of PG or nicardipine. Ratio of PaO₂ and oxygen fraction (P/F ratio) was calculated.

Results. Both PG and nicardipine decreased blood pressure similarly with increase in heart rate. P/F ratio decreased only with PG.

Conclusion. The use of prostaglandin E₁ to induce hypotension during general anesthesia is associated with a decreased PaO₂, while nicardipine has no effect. This difference in effect on PaO₂ is important in selecting an agent to induce hypotension in neurosurgery.

Key words: Hypotension; Nicardipine; Prostaglandin E₁; Arterial oxygen pressure

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INTRODUCTION

To induce hypotension for decreasing blood loss during general anesthesia in neurosurgery, nicardipine or prostaglandin E₁ (PG) is often infused. It is usually considered that systemic vasodilation induces pulmonary vascular dilation and increases pulmonary blood flow, which increases intrapulmonary shunt.¹ Therefore, arterial

oxygen pressure (PaO₂) may decrease, which is sometimes critical in neurosurgery because brain is easily damaged by short lasting hypoxia.

In animal study, PG inhibits hypoxic pulmonary vasoconstriction, which may worsen pulmonary gas exchange.² In dogs, nicardipine decreased systemic and pulmonary vascular resistance, and increased cardiac output, intrapulmonary shunt, which

decreased PaO₂.³ In human study, PG decreased PaO₂ significantly in the adult respiratory distress syndrome.⁴ We could not find any human studies about the effects of nicardipine on PaO₂. Therefore, the present study was performed to compare the effects of nicardipine and PG induced hypotension on PaO₂ during general anesthesia for brain tumor resection.

METHODOLOGY

This is a non-blind randomized controlled study. After the approval of the ethics committee of the hospital under the standards of the Helsinki Declaration and informed consent from patients, 50 patients aged 40 to 65 years for resection of brain tumor were enrolled in this study. They were divided into five groups at random by an envelope method. Those who had respiratory, cardiac, renal, or liver diseases, and who had taken prostaglandin, or calcium antagonists before surgery were excluded.

Without any premedication, anesthesia was induced with midazolam 0.1 mg/kg, fentanyl 4 µg/kg, and endotracheal intubation was facilitated with vecuronium 0.15 mg/kg. Anesthesia was maintained with oxygen 2 L/min, nitrous oxide 4 L/min, isoflurane 0.5 to 1.0 %, and fentanyl 6 to 10 µg/kg (including induction dose). Radial artery was cannulated to measure blood pressure and arterial

blood gas. Lactated Ringers solution was infused at 4 – 5 ml/kg/h and to keep urine volume more than 1 ml/kg/h. Twenty % mannitol 300 ml was infused just after craniotomy. Ventilation was adapted to keep end-tidal carbon dioxide tension (EtCO₂) between 30 and 35 mmHg.

After microsurgical procedure started and when blood pressure and heart rate were stable as ±5% variation for 30 min, administration of PG 0.05 µg/kg/min (Group PG0.05), PG 0.1 µg/kg/min (Group PG0.1), nicardipine 0.5 µg/kg/min (Group N0.5), or nicardipine 1.0 µg/kg/min (Group N1) started and stopped at two hours later in 10 patients each. Another 10 patients were served as the control without infusion of any vasodilators.

Arterial blood pressure, heart rate, percutaneous oxygen saturation (SpO₂), EtCO₂, PaO₂, and PaCO₂ were measured every 5 min until 90 min after stop of administration of PG or nicardipine. PaO₂ / FIO₂ (fraction of inspiratory oxygen) was calculated as P/F ratio.

Data were shown as mean ± standard deviation or number of patients. Power analysis was performed to detect the intra- and inter- group differences of measured parameters with power of 0.95 and effect size of 0.25 using G Power™ software.⁵ Statistical analysis was performed with the chi-square test and factorial analysis of variance (ANOVA) for

Table 1: Demographic data of the patients

Parameter	Control	PG0.05	PG0.1	N0.5	N1
Age (years)	53 ± 8	58 ± 7	52 ± 5	55 ± 8	54 ± 6
Gender (Male/Female)	5/5	7/3	4/6	6/4	4/6
Body weight (kg)	59 ± 7	62 ± 8	60 ± 9	57 ± 6	59 ± 6
Height (cm)	162 ± 6	158 ± 8	160 ± 6	159 ± 7	164 ± 7
Duration of surgery (min)	485 ± 74	427 ± 63	466 ± 69	493 ± 80	448 ± 78

Legend: PG0.05, prostaglandin E₁ 0.05 µg/kg/min; PG0.1, prostaglandin E₁ 0.1 µg/kg/min; N0.5, nicardipine 0.5 µg/kg/min; N1, nicardipine 1 µg/kg/min
Data shown as mean ± standard deviation

Table 2: Data showing isoflurane use

Parameter	Control	PG0.05	PG0.1	N0.5	N1
Isoflurane consumption (MAC.h)	7.5 ± 2.0	6.8 ± 1.8	7.1 ± 2.2	7.7 ± 2.3	6.7 ± 2.1
Maximum isoflurane concentration (MAC)	1.4 ± 0.3	1.2 ± 0.4	1.1 ± 0.3	1.2 ± 0.3	1.3 ± 0.2
Minimum isoflurane concentration (MAC)	0.6 ± 0.1	0.5 ± 0.2	0.6 ± 0.2	0.7 ± 0.2	0.6 ± 0.3

Legend: PG0.05, prostaglandin E₁ 0.05 µg/kg/min; PG0.1, prostaglandin E₁ 0.1 µg/kg/min; N0.5, nicardipine 0.5 µg/kg/min; N1, nicardipine 1 µg/kg/min; MAC, minimum alveolar concentration
Data shown as mean ± standard deviation

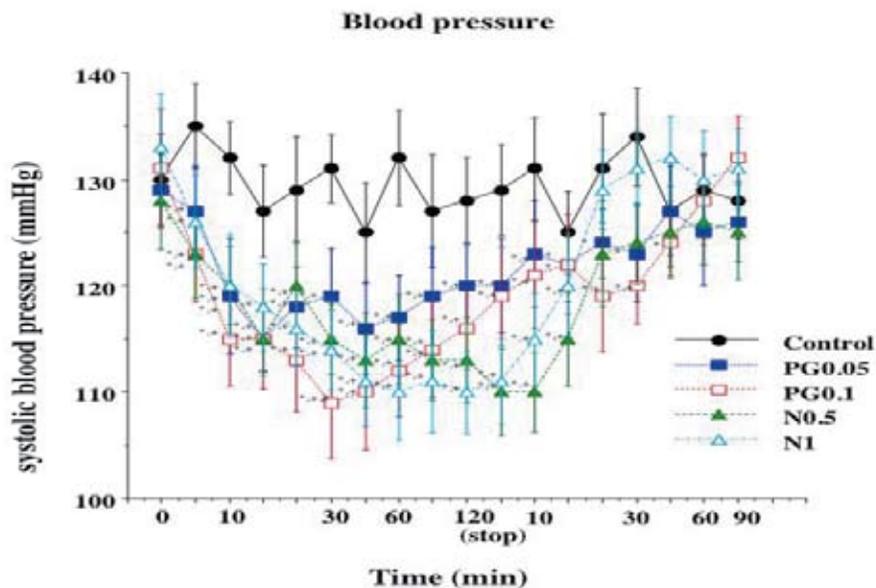


Figure 1: Comparison of blood pressure in the groups

Mean \pm standard deviation; PG0.05, prostaglandin E₁ 0.05 μ g/kg/min; PG0.1, prostaglandin E₁ 0.1 μ g/kg/min; N0.5, nicardipine 0.5 μ g/kg/min; N1, nicardipine 1 μ g/kg/min; *, P < 0.05 vs. the value at time 0; +, P < 0.05 vs. the value of the Control group

Figure 2: Comparison of heart rate in the groups

Mean \pm standard deviation; PG0.05, prostaglandin E₁ 0.05 μ g/kg/min; PG0.1, prostaglandin E₁ 0.1 μ g/kg/min; N0.5, nicardipine 0.5 μ g/kg/min; N1, nicardipine 1 μ g/kg/min; *, P < 0.05 vs. the value at time 0; +, P < 0.05 vs. the value of the Control group

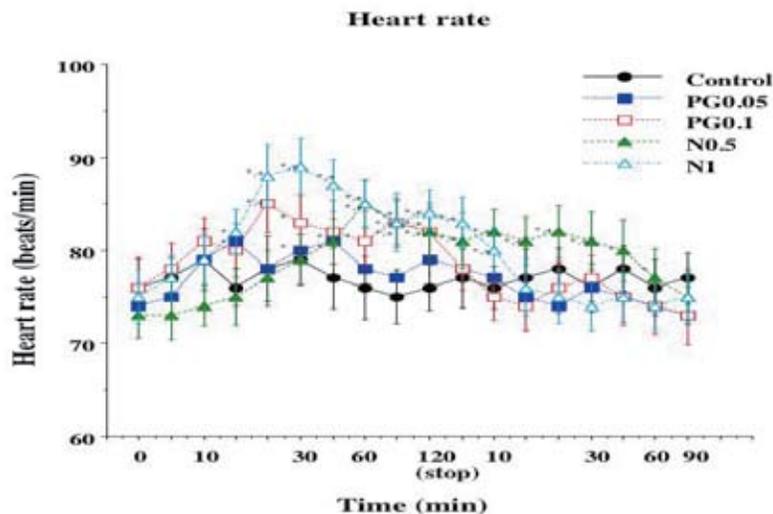
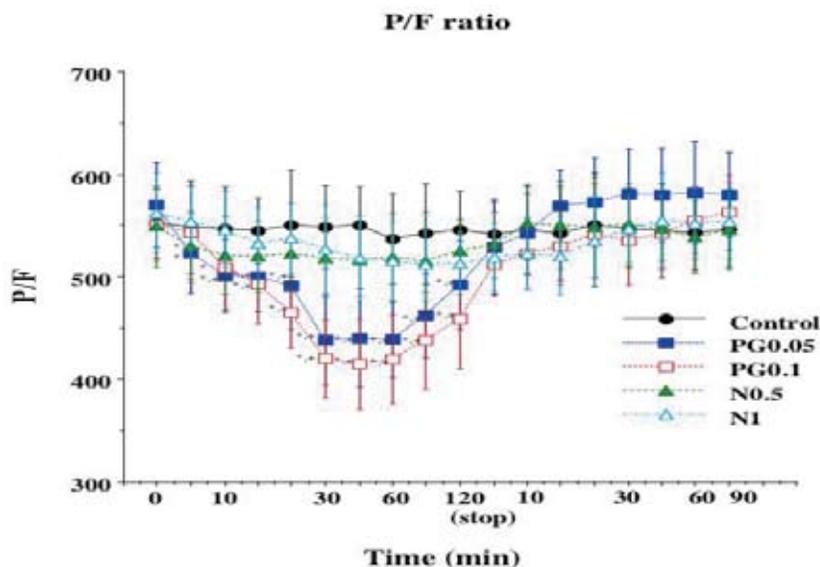


Figure 3: Comparison of P/F ratio in the groups

PaO₂/FIO₂; Mean \pm standard deviation; PaO₂, arterial oxygen pressure; FIO₂, fraction of inspiratory oxygen; PG0.05, prostaglandin E₁ 0.05 μ g/kg/min; PG0.1, prostaglandin E₁ 0.1 μ g/kg/min; N0.5, nicardipine 0.5 μ g/kg/min; N1, nicardipine 1 μ g/kg/min; *, P < 0.05 vs. the value at time 0; +, P < 0.05 vs. the value of the Control group



demographic data, and repeated ANOVA for measured parameters followed by Student-Neuman-Keuls test as a post hoc analysis. A p value less than 0.05 was considered to be statistically significant.

RESULTS

By the power analysis, 50 patients had enough power to detect the difference. Demographic data were not different among the five groups (Table 1). Isoflurane usage was not different between the two groups (Table 2).

PG decreased blood pressure dose dependently and returned to the control level in 30 min after stop of administration in Group PG0.05 and in 45 min in Group PG0.1 (Figure 1). Both Group N0.5 and Group N1 had the same level of blood pressure decrease, and blood pressure returned to the control level in 15 min after stop of administration in both Groups N0.5 and N1.

Heart rate increased in all groups (Figure 2). Group N1 had its peak increase at 30 min and returned to the control level in 10 min after stop of administration. Group N0.5 had its peak increase at 60 min and returned in 60 min after stop of administration. PG0.1 group had its peak increase at 20 min and returned in 60 min after start of administration. PG0.05 group had its peak increase at 15 min and returned in 45 min after start of administration.

SpO₂ was $\geq 98\%$ in every patient and did not have any differences among the groups. EtCO₂ was in the range between 30 and 35 mmHg during the study in all patients. P/F ratio decreased only in Groups PG0.05 and PG0.1 with its peak decrease at around 45 min after start of administration, and returned to the control levels in 5 min after stop of administration (Figure 3).

DISCUSSION

There are some animal experiments of the effects of PG on PaO₂. In dogs, PG inhibited hypoxic pulmonary vasoconstriction induced by vasodilation at 5 $\mu\text{g}/\text{kg}/\text{min}$ but not at 1.25 $\mu\text{g}/\text{kg}/\text{min}$.⁶ PG 0.2 to 0.4 $\mu\text{g}/\text{kg}/\text{min}$ decreased pulmonary vascular resistance and shunt, and increased PaO₂ in dogs.⁷ Oxygen delivery remained unchanged or increased since the cardiac index increased with PG 0.025 to 0.1 $\mu\text{g}/\text{kg}/\text{min}$ during one-lung ventilation in pigs.⁸ From these animal experiments, the doses of PG used in the present study might increase PaO₂ by decreasing shunt and increasing cardiac output.

However, our present clinical results showed the decrease in PaO₂ (P/F ratio) with PG 0.05 $\mu\text{g}/\text{kg}/\text{min}$ and 0.1 $\mu\text{g}/\text{kg}/\text{min}$.

In human studies, PG induced systemic hypotension and increased intrapulmonary shunt after heart transplantation.⁹ Naeije et al.¹⁰ showed that PG 0.02 to 0.04 $\mu\text{g}/\text{kg}/\text{min}$ is a potent pulmonary vasodilator with minimal effects on gas exchange in pulmonary hypertension secondary to chronic obstructive pulmonary disease. PG 0.007 to 0.135 $\mu\text{g}/\text{kg}/\text{min}$ decreased pulmonary arterial pressure, pulmonary vascular resistance, and pulmonary capillary wedge pressure, but did not change intrapulmonary shunt during surgery in patients with pulmonary hypertension.¹¹ However, Melot et al. showed that PG 0.02 to 0.04 $\mu\text{g}/\text{kg}/\text{min}$ increased shunt with no significant change in the pattern of ventilation-perfusion ratio (V_A/Q) distribution, decreased PaO₂ significantly in the adult respiratory distress syndrome.⁴ These studies have been done in patients with pulmonary hypertension and showed different results provably due to different severity of pulmonary hypertension. However, our study was performed in patients without pulmonary hypertension, and PaO₂ decreased, maybe by increased shunt.

In dogs, nicardipine decreased systemic and pulmonary vascular resistance, and increased cardiac output, intrapulmonary shunt, which decreased PaO₂.³ In addition, nicardipine decreases PaO₂ due to ventilation-perfusion mismatch by inhibition of hypoxic pulmonary vasoconstriction induced by vasodilation. However, nicardipine increases cardiac output, which increases oxygen delivery.¹² In human study,¹³ nicardipine does not dilate pulmonary vessels, and does not increase pulmonary shunt. Therefore, PaO₂ did not decrease with nicardipine in the present study.

CONCLUSION

In conclusion, to induce hypotension in general anesthesia for neurosurgery, the use of prostaglandin E₁ is associated with a decreased PaO₂, while nicardipine has no effect. This difference in effect on PaO₂ is important in selecting an agent to induce hypotension in neurosurgery.

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Conflict of interest: None declared.

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