J Anesth (1994) 8:154–158

Journal of
Anesthesia

Effects of prostaglandin E_1 on renal hemodynamics

ATSUKO KOBAYASHI

Department of Anesthesiology, Kyoto Prefectural University of Medicine, 465 Kajiicho, Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto, 602 Japan

Abstract: The glomerular filtration rate (GFR), renal plasma flow (RPF), renal blood flow (RBF), filtration fraction (FF), and the ratio of mean arterial pressure (MAP) to RBF (MAP/RBF), reflecting renal vascular resistance (RVR) were determined to investigate the effects of intravenously administered prostaglandin E_1 (PGE_1) on renal hemodynamics in humans. PGE_1 produced no significant changes in GFR, but did cause significant increases in RPF and RBF and significant decreases in FF and MAP/RBF. The relationships between MAP and GFR, MAP and RBF, and MAP and MAP/RBF were investigated. PGE_1 suppressed the increase of MAP/RBF along with the increase of MAP, increased the RBF along with the increase of MAP, and kept the GFR constant, regardless of MAP. Also, the effects of PGE_1 on renal pericapillary vessels were simulated. According to this simulation, PGE_1 had a vasodilator action on both preglomerular and postglomerular capillaries.

Key words: Renal hemodynamics, Prostaglandin E_1, Glomerular filtration rate, Renal blood flow, Renal vascular resistance, Mean arterial pressure

Introduction

Prostaglandin E_1 (PGE_1), often used to induce hypotension during anesthesia, is also thought to increase renal blood pressure and urinary volume [1–3]. This effect reduces the decrease of renal blood pressure and of Na excreted under the stress of surgery and anesthesia and, therefore, is considered to be effective in maintaining urinary volume during induced hypotension [4–6]. This study was carried out to elucidate the effects of PGE_1 on renal hemodynamics.

Address correspondence to: A. Kobayashi
Received for publication on April 14, 1993; accepted on August 6, 1993

In this study, glomerular filtration rate (GFR) and renal blood flow (RBF) showed different reactions to the administration of PGE_1, 0.03 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Since the difference in the reaction of afferent and efferent arterioles to PGE_1 was thought to be a possible explanation of the difference in the reaction of GFR and RBF, the vascular resistance of afferent arterioles (Ra) and efferent arterioles (Re) were simulated to provide a more detailed explanation of the mechanism of PGE_1.

Materials and methods

The subjects of this study were 11 ASA class I~II patients, six men and five women, with a mean age of 40.6 years, scheduled for elective orthopedic or cranial surgery. Informed consent was obtained from each patient, and the study was approved by the Hospital Ethics Committee. None had clinical evidence of renal disease. Patients served as their own controls.

All patients were premedicated with atropine (0.5 mg, im) and hydroxyzine (50 mg, im) 30 min before induction of anesthesia. Anesthesia was induced with thiopental (5 $mg \cdot kg^{-1}$, iv) and pancuronium (0.1 $mg \cdot kg^{-1}$, iv) and was maintained with enflurane (0.5~2.0%) and nitrous oxide (67%) in oxygen. After induction of anesthesia, the left radial artery was cannulated for measurement of arterial blood pressure and sampling of arterial blood. Mannitol (5 $ml \cdot kg^{-1}$) was infused intravenously to maintain urinary volume within 15 min after intubation. Lactated Ringer's solution was infused at a rate of 10 $mg \cdot kg^{-1} \cdot h^{-1}$ throughout this study.

To evaluate RBF, 15 ml of 3% para-aminohippuric acid (PAH) was infused intravenously for 6 min, at 150 $ml \cdot h^{-1}$, after the induction of anesthesia. Then 80 ml of 3% PAH was infused intravenously at 20 $ml \cdot h^{-1}$ for the subsequent period. Blood and urine were sampled at 30-min intervals until 2 h after PAH administration to determine the concentrations of PAH and en-

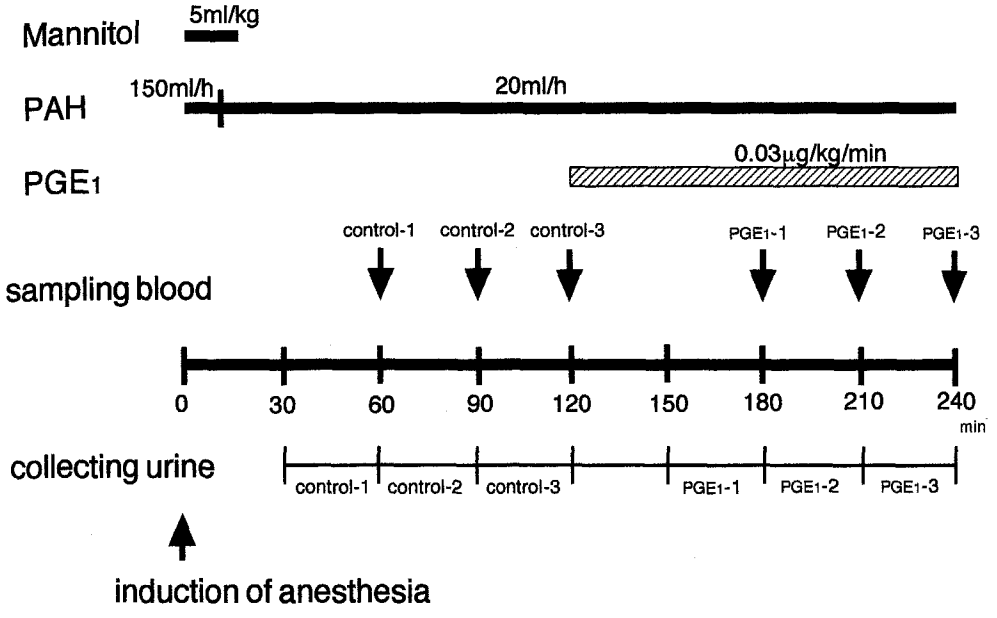


Fig. 1. Study protocol

dogenous creatinine (control group), respectively. Thereafter, a continuous infusion of PGE_1, 0.03 $\mu g \cdot kg^{-1} \cdot min^{-1}$, was begun. Blood and urine were sampled 30 min after the PGE_1 infusion in the same manner as the control group (PGE_1 group). GFR was determined from the rate of endogenous creatinine clearance, and renal plasma flow (RPF) using the rate of PAH clearance. RBF was calculated by RPF and hematocrit values, and the filtration fraction (FF) as the ratio of GFR to RPF. GFR, RPF, and RBF were normalized by dividing each value ($ml \cdot min^{-1}$) by body surface area (BSA). A block diagram of the study protocol is shown in Fig. 1. The results were expressed as mean ± SD and a paired *t*-test was used for statistical analysis. A *P* value less than 0.05 was considered statistically significant.

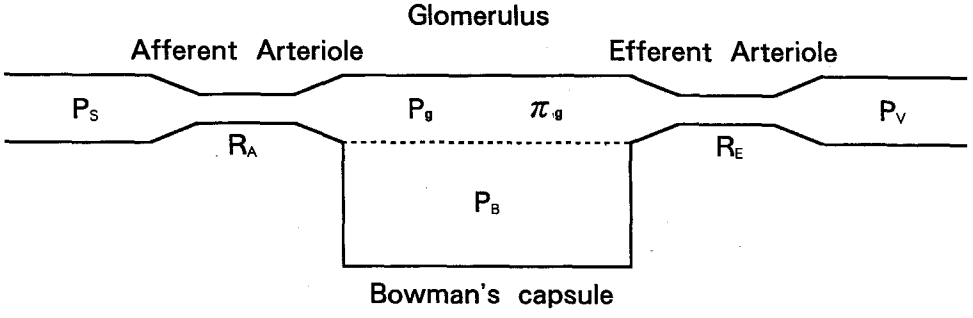
Simulation

GFR can be expressed by the following formula:

$$GFR = Kf(Pg - Pb - \pi g) \quad (1)$$

where Kf is the glomerular filtration coefficient, Pg is the glomerular hydrostatic pressure, Pb is the hydrostatic pressure in Bowman's capsule, and πg is plasma colloid osmotic pressure along the capillary (Fig. 2).

Assuming there was no marked change in Pb, and that the change in πg was small enough to be ignored in comparison with the changes in Pb and Pg, Kf and Pg were almost constant because GFR was constant. It was



$$GFR = Kf\ (P_g - P_B - \pi_g) \qquad P_g = 50$$

$$RVR = R_A + R_E \qquad R_E = RVR \times \frac{P_g}{P_S}$$

$$P_g = P_S \times \frac{R_E}{R_A \times R_E} \qquad R_A = RVR \cdot R_E$$

Fig. 2. Simulation of the glomerulus and the periglomerular capillaries

therefore assumed that Pg was constant at 50 mmHg [7].

Renal vascular resistance (RVR), Pg, and RBF are expressed in the following formulas:

$$RVR = Ra + Re \quad (2)$$

$$Pg = MAP \times Re/(Ra + Re) \quad (3)$$

$$RBF = MAP/RVR \quad (4)$$

where Re is the vascular resistance of efferent arterioles, Ra is the vascular resistance of afferent arterioles, and MAP is the mean arterial pressure. RVR, Re, and Ra were calculated by solving equations (2), (3), and (4) simultaneously. The correlation between RVR, Re, Ra, and MAP was then examined.

Table 1. Comparison of mean arterial pressure (MAP) and renal hemodynamics before and after prostaglandin E_1 (PGE_1) administration

	Control group (n = 11)	PGE_1 group (n = 11)
MAP (mmHg)	89.2 ± 15.3	78.7 ± 12.8*
Urinary volume (ml/BSA)	87.5 ± 15.8	62.5 ± 18.1*
GFR (ml/min/BSA)	45.1 ± 18.8	46.6 ± 15.3
RPF (ml/min/BSA)	165.3 ± 48.1	249.4 ± 111.6*
RBF (ml/min/BSA)	242.5 ± 70.2	370.3 ± 155.6*
FF	0.33 ± 0.20	0.20 ± 0.08*
MAP/RBF	0.40 ± 0.15	0.25 ± 0.13*

Values are expresed as mean ± SD.
GFR, glomerular filtration rate; RPF, renal plasma flow; RBF, renal blood flow; FF, filtration fraction.
* $P < 0.05$ significantly different from the control group.

Results

The results are summarized in Table 1. MAP decreased significantly (11.8%) after administration of PGE_1 at the rate of 0.03 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Urinary volume decreased significantly (28.6%) from 87.5 ± 15.8 ml·BSA^{-1} to 62.5 ± 18.1 ml·BSA^{-1}.

The PGE_1 group and control group did not differ significantly as to GFR. Both RPF and RBF increased significantly after administration of PGE_1. Because of the lack of change in GFR and the increase in RPF, these resulted in a decrease in FF from 0.33 ± 0.20 to 0.20 ± 0.08. The ratio MAP to RBF (MAP/RBF) reflecting renal vascular resistance (RVR), decreased significantly in the PGE_1 group.

Figure 3 shows the correlation between MAP and GFR, and between MAP and RBF. In the control group, GFR and RBF were regulated from 40 to 50 ml·min^{-1}·BSA^{-1} and at 250 ml·min^{-1}·BSA^{-1}, respectively, as MAP ranged from 60 to 120 mmHg. MAP/RBF, reflecting RVR increased with MAP. In contrast, in the PGE_1 group, GFR was regulated from 40 to 50 ml·min^{-1}·BSA^{-1}, and RBF increased along with MAP, as MAP ranged from 60 to 120 mmHg. MAP/RBF remained constant regardless of MAP.

In the control group, RVR increased along with MAP. According to this simulation, this increase was caused mainly by an increase in Ra, while Re remained almost constant (Fig. 4). In the PGE_1 group, RVR showed no marked change when MAP was between 60 and 120 mmHg. This simulation shows that this constancy resulted from an increase in Ra and a decrease in Re as MAP increased; RVR, the sum of Ra and Re, remained almost constant.

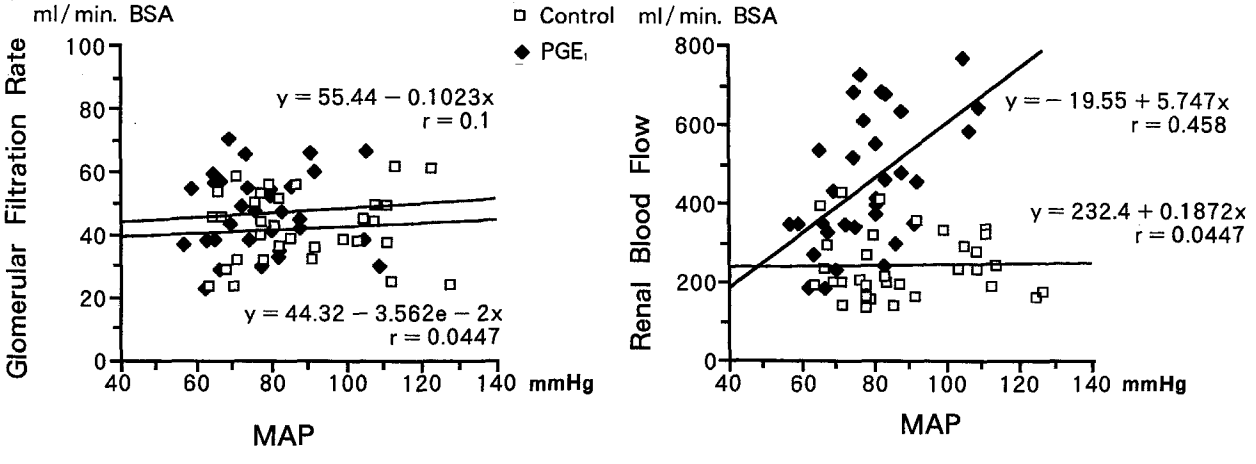


Fig. 3. Correlation of mean arterial pressure (*MAP*) and renal hemodynamics before and after prostaglandin E_1 (PGE_1) administration

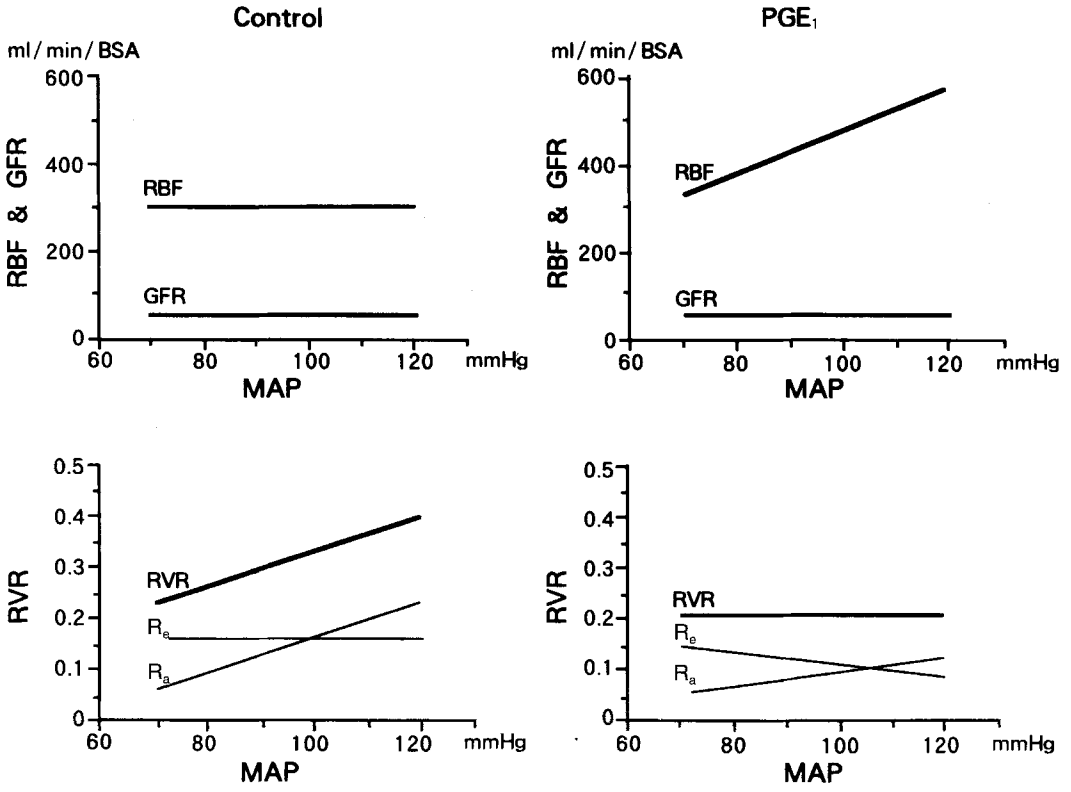


Fig. 4. Comparison of renal hemodynamics before and after PGE_1 administration. *RBF*, renal blood flow; *GFR*, glomerular filtration rate; *RVR*, renal vascular resistance

Discussion

It is generally accepted that RBF and GFR are constant regardless of MAP in a normal kidney (autoregulation) [7]. Autoregulatory responses are mediated by the active adjustment of smooth muscle tone. This autoregulation is controlled mainly by changing arterial resistance at the preglomerular site. This Ra adjustment enables the kidneys to keep Pg and GFR constant [8,9]. In a healthy, normal kidney, Ra exceeds Re when MAP increases above 100 mmHg, so that an increase in GFR is suppressed regardless of MAP. Re exceeds Ra when MAP decreases below 100 mmHg. This tendency prevents a decrease in renal perfusion pressure and keeps GFR constant. An increase in RVR along with MAP suppresses increase in RBF along with MAP.

As shown in Fig. 4, in the control group, RVR increased along with MAP and GFR and RBF were constant even during general anesthesia. According to this simulation, the adjustment of smooth muscle tone remained effective under general anesthesia. In contrast, the administration of PGE_1 suppressed the increase in RVR and increased RBF while keeping GFR constant. The constant GFR and increasing RBF suggest an increase in blood flow in peritubular capillaries. A previous study [10] has revealed that exogenous PGEs increase renal medullary blood flow, and protect renal tubular cells from the damage due to low perfusion in shock. PGE_1 is thought to prevent postischemic renal failure [11–13] and to protect renal cells during induced hypotension, since PGE_1 decreases the release of enzymes (*N*-acetyl-β-glucosaminidase, γ-glutamyl transpeptidase) in the urine [14].

According to this simulation, both Ra and Re decrease after the administration of PGE_1, but Ra exceeds Re at a MAP of 100 mmHg. Decreases in Ra and Re after the administration of PGE_1 lead to an increase in hydrostatic pressure in the peritubular capillaries. Because the decrease in Ra is greater than that in Re, both RPF and GFR are increased. At the same time, however, a decrease in Re suppresses any increase in GFR. Thus, PGE_1, by means of changes in Ra and Re, keeps the increase in GFR relatively smaller than that in RPF. This difference results in a decrease in FF, more plasma flow in postglomerular vessels, and a decrease in the plasma protein concentration, i.e., plasma colloid osmotic pressure. The increase in hydrostatic pressure and the decrease in plasma colloid osmotic pressure of peritubular capillaries, derived from the decreases in Ra and Re, decrease the intake of fluid into peritubular capillaries. This series of phenomena may be one of the

reasons PGE_1 decreases sodium reabsorption and increases urinary volume [15–17].

One of the possible protective mechanisms of PGE_1 may be related to the inhibition of preglomerular vasoconstriction. During general anesthesia, under various kinds of stresses, the endogenous prostaglandin system and the renin-angiotensin system are already activated, leading to a prostaglandin-dependency of kidney functions. Angiotensin (ANG) II acts mainly on efferent arterioles [18–20], whereas PGE_1 is thought to dilate both afferent and efferent arterioles. McGiff et al. [21] suggested that endogenous prostaglandin E group (PGEs) is an important factor in controlling the decrease in RBF induced by ANG II, because PGEs provide an action antagonistic to that of ANG II. This concept is supported by the fact that cyclooxygenase antagonists such as indomethacin enhance the renal vasoconstriction induced by ANG II [22,23]. This may be another reason why PGE_1 maintains urinary volume during induced hypotension.

Microscopic observation of efferent and afferent arterioles may permit a direct assessment of the effects of PGE_1 on renal microcirculatory dynamics [1,24,25]. RBF under general anesthesia is decreased by stress; additional decreases may lead to renal failure postoperatively. PGE_1 can improve renal function during induced hypotension.

References

1. Vander AJ (1968) Direct effects of prostaglandin on renal function and renin release in anesthetized dog. Am J Physiol 214: 218–221
2. Orloff J, Handler JS, Bergstorm S (1965) Effect of PGE_1 on the permeability response of toad bladder to vasopressin, theophylline and adenosine 3′,5′-monophosphate. Nature 205:387
3. Johnston HH, Herzoy JP, Lauler DP (1967) Effect of PGE_1 on renal hemodynamics, sodium and water excretion. Am J Physiol 213:939–946
4. Goto F, Fujita T (1980) Prostaglandins and renal dysfunction (in Japanese). Rinsho Masui (J Clin Anesthesiol) 4:1
5. Otani E, Goto F (1981) Study of hypotensive anesthesia induced by PGE_1 (in Japanese). Rinsho Masui (J Clin Anesthesiol) 5:1291–1297
6. Yoshimine K, Oba T, Yoshimura N (1981) Clinical application of Prostaglandin E_1 for hypotensive anesthesia (in Japanese, with English abstract), Masui (Jpn J Anesthesiol) 15:664–671
7. Navar LG, Carmines PK, Paul RV (1989) Renal circulation. In: Massry SG, Glassock RJ (eds) Textbook of nephrology, 2nd edn. Williams and Wilkins, Baltimore, pp 43–53
8. Fray JCS, Lush DJ, Park CS (1986) Interrelationship of blood flow, juxtaglomerular cells and hypertension: role of physical equilibrium and Ca^{2+}. Am J Physiol 251:R643–R662
9. Romero JC, Knox FG (1988) Mechanisms underlying pressure-related natriuresis: the role of the renin-angiotensin and prostaglandin systems. Hypertension 11:724–738
10. Yoshida M, Ueda S, Soejima H, et al. (1986) Effects of prostaglandin E_2 and I_1 on renal cortical and medullary blood flow in rabbits. Arch Int Pharmacodyn Ther 282:108–117
11. Ohyabu Y (1984) A study of comparison of method for the preservation in the warm ischemic kidney (in Japanese, with English abstract), Kurume Igakkai Zasshi (J Kurume Med Assoc 47:1530–1546
12. Torsello G, Schror K, Szabo Z, et al. (1989) Effects of prostaglandin E_1 (PGE_1) on experimental renal ischemia. Eur J Vasc Surg 3:5–13
13. Moskowitz PS, Korobkin M, Rambo ON (1975) Diuresis and improved renal hemodynamics produced by prostaglandin E_1 in the dog with norepinephrine-induced acute renal failure. Invest Radiol 10:284–299
14. Kumagai K, Nakada K, Kikuchi K (1989) Effect of induced hypotension on the damage of renal tubular cells (in Japanese, with English abstract), Masui (Jpn J Anesthesiol) 38:1317–1322
15. Dagharty TM, Belleau LJ, Martino JA, et al. (1968) Interrelationship of physical factors affecting sodium reabsorption in the dog. Am J Physiol 215:1442–1447
16. Shimizu K, Kurosawa T, Maeda T, et al. (1969) Free water excretion and washout of renal medullary urea by prostaglandin E_1. Jpn Heart J 10:437–455
17. Earley LE, Daugharty TM (1969) Sodium metabolism. N Engl J Med 281:72–86
18. Dunn MJ (1983) In: Dunn MJ (ed) Renal endocrinology. Williams and Wilkins, Baltimore, pp 1–74
19. Mendelsohn FAO (1982) Angiotensin II: Evidence for its role as an intrarenal hormone. Kidney Int 22:578–581
20. Edwards RM (1983) Segmental effects of norepinephrine and angiotensin II on isolated renal micro vessels. Am J Physiol 244:F526–F534
21. McGiff JC, Crowshaw K, Terrango NA, et al. (1970) Release of prostaglandin-like substance into renal venous blood in response to angiotensin II Circ Res 26–27 1(Suppl. I):121–130
22. Aiken JW, Vane JR (1973) Internal prostaglandin release attenuates the renal vasoconstrictor activity of angiotensin. J Pharmacol Exp Ther 184:678–687
23. Negus P, Tannen RL, Dunn MJ (1976) Indomethacin potentiates the vasoconstrictor actions of angiotensin II in normal man. Prostaglandins. 12:175–180
24. Edwards RM (1985) Effects of prostaglandins on vasoconstrictor action in isolated renal arterioles. Am J Physiol 248:F779–F784
25. Navar LG, Gilmore JP, Joyner WL (1986) Direct assessment of renal microcirculatory dynamics. Fed Proc 45:2851–2861