# The Effects of Prolonged Controlled Hypotension Induced by Prostaglandin $E_1$ on Renal Tubular Function

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The effects of the prolonged 3-hour and 6-hour controlled hypotension induced by prostaglandin $E_1$ ($PGE_1$) on renal tubular function have been comparatively studied with trimethaphan (TMP; 3-hour hypotensive anesthesia) and enflurane deep anesthesia (6-hour hypotensive anesthesia), using the urine N-acetyl-$\beta$-D-glucosaminidase (NAG index) and the serum and urine $\beta_2$-microglobulin (fractional clearance of $\beta_2$-m; Fc-$\beta_2$-m) as markers. During 3-hour and 6-hour controlled hypotension $PGE_1$, NAG index and Fc-$\beta_2$-m and urine volume could be maintained without remarkable changes. In the group with TPM, NAG index and Fc-$\beta_2$-m significantly increased. The increasing trend was also noted over time in deep anesthesia with enflurane. On 1st postoperative day, Fc-$\beta_2$-m significantly increased in $PGE_1$ group in both 3-hour and 6-hour hypotensive anesthesia, whereas it restored to normal on 2nd postoperative day. Also, in TMP and enflurane deep anesthesia, Fc-$\beta_2$-m significantly increased on 1st postoperative day. With the latter, significant increase was also observed on 2nd postoperative day. These results suggest that, in 3-hour and 6-hour controlled hypotension induced by $PGE_1$, renal tubular function is normally maintained and that it is useful for prolonged controlled hypotensive anesthesia. However, further study is necessary because tubular dysfunction might appear on 1st postoperative day. (Key words: prolonged controlled hypotension, renal tubular function, urine NAG index, fractional clearance of $\beta_2$-microglobulin (Fc-$\beta_2$-m))

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For the maxillo-facial surgery, much time is required and massive blood transfusion is also needed because heavy bleeding occurs. The patients of this surgical procedure are relatively young, and it appears to be essential to reduce the bleeding during operation and to save the transfusion blood. The simultaneous application of controlled hypotensive anesthesia is useful for this purpose[1–4]. One of the problems of the controlled hypotensive anesthesia is the maintenance of the blood flow to the important organs under hypotension, and this is influenced by the types of hypotensive agents, and by the degree and the duration of hypotension. Most of the reports describing the influence of the controlled hypotensive anesthesia on the blood flow to organs have been based on the data obtained under hypotension with systolic blood pressure at about 80 mmHg and the duration of 1–2 hr[5–8], and very few studies have been performed on data under hy-

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potension for 3 hr or more. For the maxillofacial surgery under the present study, the prolonged controlled hypotension of 3 hr or more is needed, and the prolonged hypotension possibly exerts influence on the maintenance of blood flow to the important organs and also on the postoperative functions of these organs. In this study, we performed 3-hour and 6-hour prolonged controlled hypotensive anesthesia by prostaglandin $E_1$ ($PGE_1$), in which the blood flow to the organs could be maintained under controlled hypotension. By measuring N-acetyl-$\beta$-D-glucosaminidase (NAG) and $\beta_2$-microglobulin ($\beta_2$-m) used as the markers for the disturbance of tubular reabsorption, the influence of the controlled hypotension on renal tubular function during anesthesia and after operation was comparatively studied with the controlled hypotension during with trimethaphan (TMP) and enflurane deep anesthesia.

## Patients and Methods

The study was performed on the patients, who were scheduled to undergo the maxillo-facial surgery (Le Fort II or III osteotomy and sagittal osteotomy for maxillary hypoplasia or facial bone fracture) with the scheduled operation time of 4 hr and the possible expected bleeding of 800–1000 ml and the surgery with the scheduled operation time of 7 hr and the possible expected bleeding of 1500–2000 ml. The patients of ASA I–II having no history of renal dysfunction, hypertension and anemia were selected. The informed consent was obtained from the patients and their family on the details of the study and the necessity and the problems related with the prolonged controlled hypotension in all cases.

As the premedication, 0.5 mg of atropine sulfate and 1 $mg \cdot kg^{-1}$ of hydroxydine were given intramuscularly one hour before the induction. The anesthetic induction was performed with GO-NLA ($O_2$ 33%, $N_2O$ 67%, droperidol 0.25 $mg \cdot kg^{-1}$, fentanyl 5.0 $\mu g \cdot kg^{-1}$). After muscular relaxation was attained with 0.1 $mg \cdot kg^{-1}$ of pancronium, oral or nasotracheal intubation was performed. For the maintenance of anesthesia, 0.5 0.7% enflurane was used, and fentanyl and pancronium were given as appropriate. $Pa_{CO_2}$ was kept at 35–40 mmHg by the controlled respiration. For all cases, $Sa_{O_2}$, $P_{ET_{CO_2}}$ and the end-expiratory concentration of enflurane were monitored, and the arterial pressure was invasively measured and recorded from radial artery. A catheter to measure central venous pressure was inserted from ulnar cutaneous vein or femoral vein. Before the operation, the controlled hypotensive anesthesia was started by the hypotensive agents. With the systolic blood pressure of 80 mmHg as goal, $PGE_1$ or TMP were used for the 3-hour hypotension group. For the 6-hour hypotension group, $PGE_1$ or 2–3% enflurane deep anesthesia was performed. The transfusion was maintained at 6–7 $ml \cdot kg^{-1} \cdot hr^{-1}$ during the controlled hypotension. On the other hand, the lactated Ringer's solution was supplied by 1.5 times as much as the bleeding. The blood transfusion was started when bleeding exceeded 900 ml during operation, and the quantity of transfusion blood was set to 1/2 to 1/3 of the bleeding quantity. CVP was maintained at constant level as practical as possible. For both the 3-hour and 6-hour hypotension groups, blood and urine were collected before starting hypotension (control value), one hour, 2 hr, and 3 hr after starting hypotension. For 6-hour hypotension group, blood and urine were also collected 4 hr and 6 hr after. The blood and urine were also collected one hour after suspension of hypotension and on 1st postoperative day for both groups, and on 2nd postoperative day for 6-hour group. From the final urination at hospital ward, Foley catheter was retained after anesthetic induction until the controlled hypotension was started, the urine volume thus collected was used as the control. As the urine on 1st and 2nd postoperative days, one-hour urine from 6:00 to 7:00 in the morning was collected. The collected arterial blood and urine were centrifuged and were kept frozen at $-20°C$ until they were measured. As the urine NAG, the reagent kit (NAG Test Shionogi) having m-cresolsulfon-phthaleinyl-NAG as substrate

**Table 1.** Clinical characteristics of subjects

| Controlled hypotension time | | Age (years) | W.T. (kg) | O.T. (min) | T.B. (gr) | T.T. (ml) | T.D. | B.T. |
|---|---|---|---|---|---|---|---|---|
| 3-hour groups | $PGE_1$ group (n=6) | 25 ± 6.5 | 56.3 ± 6.7 | 220 ± 46 | 674 ± 168 | 2152 ± 416 | 1550 ± 432(μg) | (−) |
| | TMP group (n=6) | 30.8 ± 11.2 | 52.5 ± 4 | 229 ± 36 | 630 ± 238 | 2143 ± 250 | 301 ± 142(mg) | (−) |
| 6-hour groups | $PGE_1$ group (n=6) | 25.8 ± 7.9 | 52.8 ± 4.3 | 423 ± 52 | 982 ± 411 | 3288 ± 210 | 2275 ± 612(μg) | 3 cases |
| | Enflurane group (n=5) | 18 ± 2.1 | 54.2 ± 9 | 458 ± 93 | 1029 ± 363 | 3604 ± 424 | | 3 cases |

Values are mean ± SD

Abbreviation: W.T. = weight, O.T. = operation time, T.B. = total bleeding
T.T. = total transfusion, T.D. = total drugs, B.T. = blood transfusion

was used, and the serum and urine $\beta_2$-m was measured by radioimmunoassay. To compensate the urine volume, the value of urine NAG divided by urine creatinine was used as urine NAG index. To study the handling of $\beta_2$-m value in renal tubule in more detail, the clearance of $\beta_2$-m divided by creatinine clearance, i.e. the fractional clearance of $\beta_2$-m (Fc-$\beta_2$-m) was obtained. In addition, the ratio of Na excretion (FeNa) and the free water clearance ($C_{H_2O}$) were calculated. These indices have been calculated as follows:

Urine NAG index (unit/g·creatinine)
= Urine NAG/Urine creatinine

$$\text{Fc-}\beta_2\text{-m} = \frac{\text{Urine } \beta_2\text{-m} \cdot \text{Serum creatinine}}{\text{Serum } \beta_2\text{-m} \cdot \text{Urine creatinine}}$$

$$\text{FeNa (\%)} = \frac{\text{Urine Na/Serum Na}}{\text{Urine creatinine/Serum creatinine}}$$

$$C_{H_2O}\ \text{(ml/min)} = \left(1 - \frac{\text{Urine osmol}}{\text{Plasma osmol}}\right) \times \text{Urine volume}$$

For the statistical analysis, Student's t-test (paired t-test when paired, and unpaired t-test when not paired) was used, and $P < 0.05$ was regarded as significant difference.

## Results

In the clinical characteristics of the subjects, there was no significant difference in age, body weight, total bleeding and total transfusion between the 3-hour hypotension group with $PGE_1$ and the TMP group and between the 6-hour hypotension group with $PGE_1$ and the enflurance deep anesthesia group. No blood transfusion was needed for the 3-hour hypotension group, whereas blood was transfused for three cases of the 6-hour hypotension group. In both groups, systolic pressure was maintained at 80 mmHg during hypotension, and no significant difference was noted (table 1).

*3-hour hypotension group* (table 2)

(1) Urine NAG index

In TMP group, the 2-hour and 3-hour values during hypotension and 1-hour value after suspension of hypotension significantly increased compared with the control. The 2-hour and 3-hour values during hypotension increased significantly compared with the $PGE_1$ group. On 1st postoperative day, the slightly increasing trend was observed, but there was no significant difference.

In the $PGE_1$ group, there was no remarkable change compared with the control throughout the controlled hypotension. The

**Table 2.** Markers of renal tubular function of controlled hypotension in 3-hour groups

| | pr hypo (cont) | | hypo 1h | | 2h | | 3h | | po hypo 1h | | 1POD | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | P | T | P | T | P | T | P | T | P | T | P | T |
| NAG index | 3.3 ± 1.3 | 3.7 ± 1.8 | 4.5 ± 2.0 | 9.2 ± 5.7 | 4.2 ± 1.5 | $9.0^{+}_{*}$ ± 3.7 | 3.9 ± 1.2 | $8.5^{+}_{**}$ ± 2.7 | 5.2 ± 1.9 | $6.6^{+}$ ± 1.7 | 5.2 ± 2.3 | 5.2 ± 1.4 |
| Fc-$\beta_2$-m ($\times 10^{-4}$) | 5.0 ± 2.3 | 4.3 ± 2.1 | 4.8 ± 2.8 | $8.2^{+}$ ± 2.5 | 4.9 ± 1.9 | $9.3^{+}_{*}$ ± 2.8 | 4.2 ± 2.0 | $7.7^{+}_{**}$ ± 0.6 | 6.0 ± 2.8 | $7.3^{+}$ ± 1.2 | $13.2^{+}$ ± 5.6 | $15.3^{++}$ ± 4.1 |
| FeNa (%) | 0.4 ± 0.2 | 0.5 ± 0.3 | 0.4 ± 0.2 | 0.7 ± 0.4 | 0.4 ± 0.2 | 0.7 ± 0.4 | 0.5 ± 0.3 | 0.7 ± 0.3 | 0.4 ± 0.1 | 0.7 ± 0.4 | 0.5 ± 0.2 | 0.7 ± 0.3 |
| $C_{H_2O}$ ($ml \cdot min^{-1}$) | −0.6 ± 0.4 | −0.4 ± 0.3 | −1.0 ± 0.7 | 0.4 ± 0.3 | −0.6 ± 0.4 | 0.1 ± 0.1 | −0.6 ± 0.4 | −0.3 ± 0.2 | −0.8 ± 0.6 | −0.3 ± 0.2 | 0.4 ± 0.3 | 0.1 ± 0.1 |
| U.V. (ml) | 61 ± 43 | 86 ± 37 | 78 ± 64 | $21^{+}$ ± 9 | 61 ± 37 | $37^{+}$ ± 17 | 50 ± 25 | $30^{+}$ ± 13 | 82 ± 57 | $32^{+}$ ± 21 | $188^{+}$ ± 98 | 123 ± 62 |

Values are mean ± SD

Abbreviation : pr hypo = pre hypotension, po hypo = post hypotension, cont = control
POD = Post Operative Day, P = $PGE_1$, T = TMP, U.V. = Urine Volume

$^{+}P < 0.05$, $^{++}P < 0.01$, Significant difference compared to control values

$^{*}P < 0.05$, $^{**}P < 0.01$, Significant difference compared to $PGE_1$

slightly increasing trend was noted in one-hour value after suspension of hypotension and on 1st postoperative day, but there was no significant difference.

(2) Fc-$\beta_2$-m

In the TMP group, one-hour value after suspension of hypotension and the value on 1st postoperative day increased significantly compared with the control, and the 2-hour and 3-hour values during hypotension increased significantly compared with the $PGE_1$ group.

In the $PGE_1$ group, no remarkable change was noted throughout the hypotension compared with the control. One-hour value after suspension of hypotension slightly increased, whereas it increased significantly compared with the control on 1st postoperative day.

(3) Urine volume

In the TMP group, the values during hypotension and one-hour value after suspension of hypotension significantly decreased and returned to the same level as the control on 1st postoperative day.

In the $PGE_1$ group, the values during hypotension and one-hour value after suspension of hypotension were maintained without conspicuous change compared with the control. On 1st postoperative day, the values increased significantly compared with the control.

(4) FeNa and $C_{H_2O}$

In the TMP group, FeNa increased during hypotension and on 1st postoperative day compared with the control but not significantly. The increase was 1% or less. In the $PGE_1$ group, no remarkable change was noted during the entire course. In the TMP group, $C_{H_2O}$ increased compared with the control throughout the course, but there was no significant difference. However, the absolute value was $-0.5$ $ml \cdot min^{-1}$ or more. In the $PGE_1$ group, no remarkable change occurred during hypotension. On 1st postoperative day, the values increased compared with the control, but there was no significant difference. However, the absolute value was 0.5 $ml \cdot min^{-1}$ or more.

*6-hour hypotension group* (table 3)

(1) Urine NAG index

In the enflurane deep anesthesia group, the slightly increasing trend was noted from 3-hour values during hypotension to the value on 2nd postoperative day compared with no significant difference.

In the $PGE_1$ group, there was no remarkable change in the values during hypotension and one-hour value after suspension of hypotension. On 1st postoperative day, the slightly increasing trend was seen compared with the control, but there was no significant difference.

(2) Fc-$\beta_2$-m

In the enflurane deep anesthesia group, the slightly increasing trend was observed from 3-hour value under hypotension to one-hour value after suspension of hypotension compared with the control, but there was no significant difference. On 1st and 2nd postoperative days, the values increased significantly compared with the control and the $PGE_1$ group.

In the $PGE_1$ group, no conspicuous change was noted in the values during hypotension and one-hour value after suspension of hypotension. The values increased significantly compared with the control on 1st postoperative day, whereas they restored to the same level as the control on 2nd postoperative day.

(3) Urine volume

In the enflurane deep anesthesia group, the decrease was observed from one-hour value to 4-hour value during hypotension compared with the control. Above all, 2-hour value showed significant decrease compared with the control and $PGE_1$ group. The slightly increasing trend was seen in one-hour value after suspension of hypotension and on 1st postoperative day.

In the $PGE_1$ group, there was the decreasing trend from 2-hour value to 4-hour value during hypotension compared with the control, but there was no significant difference. On 1st postoperative day, the value increased compared with the control value, but the difference was not significant.

(4) FeNa and $C_{H_2O}$

In the enflurane deep anesthesia group, FeNa increased in 6-hour value during hypotension and one-hour value after suspension of hypotension compared with the control, but there was no significant difference. In the $PGE_1$ group, the increasing trend was noted on 1st postoperative day, but there was no remarkable change otherwise. In the enflurane deep anesthesia group, $C_{H_2O}$ increased throughout the course compared with the control. Particularly, significant difference was noted in 2-hour, 3-hour and 4-hour values during hypotension and one-hour value after suspension of hypotension, and the absolute value was $-0.5$ ml·min$^{-1}$ or more. In the $PGE_1$ group, the increase was observed in one-hour value during hypotension and on 1st postoperative day compared with the control, but there was no significant difference.

## Discussion

The influence of the controlled hypotension on renal function varies according to the types of hypotensive agents, and the degree and the duration of hypotension. There have been a number of reports, describing the suppressive influence[7,9–11]. In studying the influence of the controlled hypotension on renal function, it is necessary to consider the function of glomerular filtration and the function of tubular reabsorption. These functions are placed under direct influence of anesthetic agents or hypotensive agents or under the influence of the changes in renal blood flow, and the influence of the latter has been reported to be higher. As the markers of renal tubular function, the ratio of Na excretion (FeNa)[12], the free water clearance ($C_{H_2O}$), RFI (urine Na/creatinine clearance), the ratio of P reabsorption, PSP test and Fischberg test have been used. However, these factors are more easily influenced by Na or osmotic load, and PSP test and Fischberg test are not achievable during transfusion. On the other hand, attention has been focused in recent years on NAG and $\beta_2$-m as the markers for proximal tubular function. It is generally accepted

**Table 3.** Markers of renal tubular function

| | pr hypo (cont) | | hypo 1h | | 2h | | 3h | |
|---|---|---|---|---|---|---|---|---|
| | P | E | P | E | P | E | P | E |
| NAG index | 4.8 ± 2.1 | 3.5 ± 2.0 | 5.4 ± 3.2 | 3.4 ± 1.8 | 5.2 ± 2.3 | 3.5 ± 1.4 | 5.8 ± 2.4 | 4.9 ± 1.3 |
| Fc-$\beta_2$-m ($\times 10^{-4}$) | 5.7 ± 2.0 | 4.0 ± 2.0 | 8.3 ± 2.5 | 4.3 ± 1.4 | 6.8 ± 0.9 | 4.0 ± 1.3 | 5.9 ± 1.5 | 7.3 ± 2.2 |
| FeNa (%) | 0.7 ± 0.4 | 0.4 ± 0.2 | 0.7 ± 0.4 | 0.3 ± 0.1 | 0.6 ± 0.3 | 0.2 ± 0.1 | 0.6 ± 0.3 | 0.2 ± 0.1 |
| $C_{H_2O}$ ($ml \cdot min^{-1}$) | −0.9 ± 0.5 | −1.2 ± 0.4 | −0.2 ± 0.1 | −0.5 ± 0.2 | −0.6 ± 0.6 | $-0.4^{+}$ ± 0.1 | −0.8 ± 0.6 | $-0.4^{+}$ ± 0.2 |
| U.V. (ml) | 83 ± 35 | 45 ± 21 | 78 ± 56 | 15 ± 6 | 43 ± 18 | $14^{+}_{*}$ ± 5 | 49 ± 15 | 28 ± 14 |

Values are mean ± SD
Abbreviation : P = $PGE_1$, E = Enflurane

that these markers reflect more sharply the disturbances than the former markers and are less influenced by the loads such as water, Na, etc[13–19]. Accordingly, these are reliable as the indicators of tubular function when the intraoperative and postoperative loads of transfusion are needed. NAG is a hydrolytic enzyme abundantly present in lysosome of proximal tubules. $\beta_2$-m is a low molecular weight glycoprotein, which easily passes through the glomerular basement membrane and is normally reabsorbed and catabolized almost completely through the proximal tubular epithelium. Therefore, the proximal tubular dysfunction increases the excretion of NAG and $\beta_2$-m into urine. There has been a report, stating that no difference was noted in urine NAG activities between one-day urine volume and one-hour urine volume[20], and the postoperative urine for this study was collected as a one-hour urine in early morning. In case of $\beta_2$-m, the biosynthesis of $\beta_2$-m increases in malignant neoplasmas or inflammatory disorders even when there is no tubular dysfunction, and urinary excretion increases when the maximal reabsorption capacity is surpassed. Because the cases under the present study were maxillary hypoplasia and facial bone fracture, the increase of $\beta_2$-m in urinary excretion may be regarded as the tubular dysfunction. Although the fractional clearance of $\beta_2$-m (Fc-$\beta_2$-m) was obtained in this study, it appears that this value is changed according to the progress in the disturbance of reabsorption without regard to the urine volume. Thus, the increase of this value may show the presence of proximal tubular dysfunction[22,23].

Among the hypotensive agents, it has been demonstrated that $PGE_1$ maintains renal blood flow and urine volume by the dilative action of renal vessels and the increasable action of cardiac output[24–28]. However, there is a report, asserting that this action to maintain urine volume is caused by the disturbance of tubular reasorption[29]. Because the urine volume was maintained without the fluctuation of urine NAG index and Fc-$\beta_2$-m in the present study during 3-hour and 6-hour hypotensive anesthesia by $PGE_1$, it is considered that tubular function has been maintained. This suggests that the action to maintain urine volume

of controlled hypotension in 6-hour groups

| 4h | | 6h | | po hypo 1h | | 1POD | | 2POD | |
|---|---|---|---|---|---|---|---|---|---|
| P | E | P | E | P | E | P | E | P | E |
| 5.6 | 4.6 | 5.5 | 5.5 | 5.6 | 6.0 | 7.4 | 7.7 | 6.4 | 5.4 |
| ± | ± | ± | ± | ± | ± | ± | ± | ± | ± |
| 3.5 | 2.9 | 2.5 | 2.0 | 2.1 | 1.7 | 3.0 | 2.7 | 2.1 | 0.9 |
| 5.2 | 6.9 | 6.0 | 7.9 | 8.4 | 15.3 | $30.9^{++}$ | $63.1^{++}_{**}$ | 4.4 | $31.7^{++}_{**}$ |
| ± | ± | ± | ± | ± | ± | ± | ± | ± | ± |
| 2.8 | 1.4 | 3.2 | 2.7 | 3.7 | 8.0 | 11.5 | 13.7 | 2.2 | 11.3 |
| 0.6 | 0.4 | 0.4 | 0.7 | 0.4 | 1.9 | 0.8 | 0.5 | 0.4 | 0.6 |
| ± | ± | ± | ± | ± | ± | ± | ± | ± | ± |
| 0.3 | 0.2 | 0.2 | 0.6 | 0.2 | 1.2 | 0.2 | 0.3 | 0.2 | 0.1 |
| −0.7 | $-0.3^{+}$ | −1.0 | −0.1 | −0.8 | $-0.1^{+}$ | 0.9 | −1.6 | −0.5 | −0.7 |
| ± | ± | ± | ± | ± | ± | ± | ± | ± | ± |
| 0.3 | 0.3 | 0.3 | 0.3 | 0.2 | 0.3 | 1.0 | 0.5 | 0.4 | 0.5 |
| 43 | 26 | 58 | 47 | 63 | 78 | 175 | 77 | 57 | 56 |
| ± | ± | ± | ± | ± | ± | ± | ± | ± | ± |
| 24 | 15 | 15 | 25 | 25 | 51 | 82 | 28 | 36 | 32 |

$^{+}P < 0.05$, $^{++}P < 0.01$, Significant difference compared to control values
$^{*}P < 0.05$, $^{**}P < 0.01$, Significant difference compared to $PGE_1$

during hypotension is based on the maintenance of glomerular function. However, in both the 3-hour and 6-hour hypotension groups, the urine NAG index and $C_{H_2O}$ showed the increasing trend on 1st postoperative day, while Fc-$\beta_2$-m increased significantly. This may be attributed to the influence of the controlled hypotension by $PGE_1$ or to the influence normally observed after the controlled hypotension of 3 hr or more. It has been reported that, in the former case, the swelling and the vacuolation of proximal tubular cells present in the deep layer of renal cortex, regarded as very weak to ischemic state in the controlled hypotension by $PGE_1$, and the swelling of mitochondria have been observed, even though slightly[30]. Therefore, when cellular damage is in mild degree, the hydrolytic enzymes such as NAG, showing the organic change, are not increased, and the low molecular weight glycoprotein such as $\beta_2$-m, exhibiting the functional change, is increased in urine. This may appear after operation slightly deviated in time. In the latter case, $C_{H_2O}$ and NAG showed the increasing trend and Fc-$\beta_2$-m exhibited significant increase on 1st postoperative day even in the 3-hour group with TMP and the 6-hour group in enflurane deep anesthesia. Renal blood flow may have decreased due to the increase of endocrinic hormone such as catecholamine or to the shortage of the circulating blood volume, resulting in the decrease of oxygen supply to tubular cells and leading to the disturbance of reabsorption. The results of the present study give no suggestion on the causes, but further study should be continued on this point. However, the significant increase of urine volume on 1st postoperative day reveals the influence of the disturbance of tubular reabsorption together with that of the postoperative diuretic period.

In the cases with TMP, the disturbance of tubular reabsorption may have been resulted from the starting of the controlled hypotension as suggested by the results of this study. The simultaneous significant increase of urine volume may lead to the disturbance of glomerular filtration, and this suggests the influence of the decrease in renal blood flow as reported by other researchers[9,10].

In the controlled hypotension by the enflurane deep anesthesia, the disturbance of

tubular reabsorption may appear as time elapses, and the disturbance may be extended after operation. This may be the reason why urine volume is also maintained as time elapses.

The results suggest that renal tubular function is maintained during the 3-hour and 6-hour controlled hypotension induced by $PGE_1$, and this can be adopted for prolonged hypotensive anesthesia in relatively safe manner. However, the disturbance of proximal tubular reabsorption may appear on 1st postoperative day, and further study should be continued on this problem.

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