Atrial Natriuretic Polypeptide (ANP) as Protective Agent of Renal Ischemia

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OMATA, K., MATSUI, K., SATO, D., KAMIOKI, S., OUTI, H. and ABE, K. *Atrial Natriuretic Polypeptide (ANP) as Protective Agent of Renal Ischemia*. Tohoku J. Exp. Med., 1989, **158** (4), 283-289 — The effect of atrial natriuretic polypeptide (ANP) on hemodynamics and renal function was evaluated after the reconstructive surgery of the left renal artery in a patient with renovascular hypertension secondary to Takayasu's arteritis. The reconstructive surgery was done using the femoral artery, since we were unable to obtain adequate vein segments to fit the renal artery. The femoral artery was reconstructed by her saphenous vein segments. After 30 min of the aortorenal bypass operation, α -human ANP (α -hANP) was infused intravenously for 10 min at a rate of 0.1 μ g/kg/min. Although total peripheral resistance was decreased by α -hANP infusion, blood pressure was not changed because of the increased cardiac output. Glomerular filtration rate was increased markedly with concomitant increases in urine volume and urinary excretions of sodium, potassium and phosphate. Fractional excretions of water and sodium were not changed, but fractional excretion of phosphate and potassium clearance were increased. Thus, the infusion of α -hANP markedly improved the renal function of the ischemic kidney by the reconstructive surgery of the renal artery, suggesting that α -hANP seems clinically applicable as a protective agent in renal ischemia at renovascular surgery as well as the renal transplantation. ——— atrial natriuretic polypeptide (ANP); renal ischemia; renovascular hypertension; reconstructive surgery

It is extremely important to avoid the ischemic renal damage for the preservation of renal function at the reconstructive surgery of the renal artery. Recently, atrial natriuretic polypeptide (ANP) has been shown to have potent natriuretic and vasodilating action in man (Kangawa and Matsuo 1984; Richards et al. 1985; Ishii et al. 1986; Weidmann et al. 1986). We report the effect of ANP on hemodynamics and renal function after the reconstructive surgery of the left renal artery in a patient with renovascular hypertension secondary to Takayasu's

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arteritis.

CASE REPORT

A 38 year-old female patient was admitted complaining for nausea and her blood pressure was 200/90 mmHg. There were no differences in blood pressures between the right and left upper limbs as well as the upper and lower limbs. Thoracic and abdominal aortograms showed moderate diffuse narrowing of the thoracic descending aorta extending to the proximal portion of the abdominal aorta and associated with constriction of the left subclavian artery. Isolated severe stenosis of the proximal portion of the left renal artery of about 90% with the post-stenotic dilatation was also found (Fig. 1). Glomerular filtration rate (GFR) measured by creatinine clearance was 77.7 ml/min and renal plasma flow measured by p-aminohippuric acid clearance was 407.9 ml/min. Figs. 2 and 3 show the renogram and renoscintigram respectively, exhibiting the marked hypofunction of the left kidney. High peripheral plasma renin activity with enhanced response to oral administration of captopril (50 mg) from 3.3 to 30.0 ng/ml/hr was found. Renal vein renin levels were determined by the direct renin radiometric assay using monoclonal anti-active renin antibody (Renin RIA Pasteur, Institute Pasteur De Lyon, Lyon, France). Active renin concentrations were as follows : left renal vein 96.4 ng/liter, right renal vein : 76.1 ng/liter, and inferior vena cava below renal veins : 81.2 ng/liter, indicating the hypersecretion of renin from the left kidney and the suppression of renin in the right kidney. The reconstructive surgery of the left renal artery was done under the anesthesia with nitrous

Fig. 1. Abdominal aortogram in a patient with renovascular hypertension secondary to Takayasu's arteritis.

Fig. 2. Renogram in a patient with renovascular hypertension secondary to Takayasu's arteritis.

Fig. 3. Renoscintigram in a patient with renovascular hypertension secondary to Takayasu's arteritis.

oxide plus oxygen and halothane. The left renal artery was reconstructed with her femoral artery, since we were unable to obtain adequate vein segments to fit the renal artery. The femoral artery was reconstructed by her saphenous vein segments. Pathological diagnosis was Takayasu's arteritis of the abdominal aorta in which edematous changes and the accumulation of mucopolysaccharide with vacuolation was found in the media (Fig. 4) and of the renal artery with marked stenosis of the left renal artery by the pronounced granulomatous hyperplasia (Fig. 5). No pathological change was found in the femoral artery. Immediately after the aortorenal bypass grafting of the left renal artery, we evaluated the effect of ANP on renal function. After 30 min of the control period α -human ANP (α -hANP: SUN 4936, Suntory Corporation, Osaka) was infused i.v for 10 min at a rate of $0.1 \mu\text{g/kg/min}$. Monitorings were continued for 30 min after α -hANP infusion as the recovery period. Blood pressure (BP) and pulse rate were monitored continuously through a catheter inserted into the right radial artery. Cardiac output (CO) was measured

Fig. 4. The histological structure of the abdominal aorta in a patient with renovascular hypertension secondary to Takayasu's arteritis.

Fig. 5. The histological structure of the left renal artery in a patient with renovascular hypertension secondary to Takayasu's arteritis.

TABLE 1. *Effects of α -hANP on renal function after renal artery reconstruction*

	Control	α -hANP	Recovery
BP (mmHg)	120/60	122/54	120/50
PR (bpm)	90	78	68
CO (liter/min)	4.4	4.8	3.7
TPR (dyne sec/cm ⁵)	1443	1268	1571
GFR (ml/min)	60.5	101.2	47.0
UV (ml/min)	7.0	11.0	5.3
UNaV (mEq/min)	0.588	0.891	0.469
UKV (mEq/min)	0.094	0.163	0.065
UPV (mg/min)	0.053	0.103	0.047
FEwater (%)	11.6	10.9	11.3
FENa (%)	7.2	6.5	7.4
FEp (%)	26.5	31.9	33.3
C-K (ml/min)	24.1	42.8	15.8

Control refers to a 30 min period after reconstruction, α -hANP to a 10 min period of α -hANP infusion and recovery to a 30 min period after the infusion. BP, blood pressure; PR, pulse rate; CO, cardiac output; TPR, total peripheral resistance; GFR, glomerular filtration rate; UV, urine volume; UNaV, urinary sodium excretion; UKV, urinary potassium excretion; UPV, urinary phosphate excretion; FEwater, fractional excretion of water; FENa, fractional excretion of sodium; FEp, fractional excretion of phosphate; C-K, potassium clearance.

by the thermodilution method through a catheter inserted into the pulmonary artery. A urinary catheter was placed in the bladder. Urine volume (UV), urinary output of sodium (UNaV), potassium (UKV) and phosphate (UPV) were measured in each period. Glomerular filtration rate (GFR) was measured by creatinine clearance. Table 1 summarizes the results. Although total peripheral resistance (TPR) was decreased from 1443 to 1268 dyne sec/cm⁵ by α -hANP infusion, blood pressure was not changed because of the increased cardiac output. GFR was increased markedly from 60.5 to 101.2 ml/min by the infusion with concomitant increases of urine volume and urinary excretions of sodium, potassium and phosphate. Fractional excretions of water and sodium were not changed, but fractional excretion of phosphate and potassium clearance were increased by the infusion. All these changes were returned toward the levels before α -hANP infusion in the recovery period.

Two weeks after the operation her blood pressure was returned to normal and GFR was increased from 77.7 to 96.3 ml/min. An improvement of the hypofunction of the left kidney was also confirmed by the renogram and the renoscintigram.

COMMENTS

Since it was impossible to avoid ischemic renal damage at the reconstructive surgery of the renal artery, mannitol and furosemide are generally administered as protective agents before and/or after the reconstructive surgery (Manninga et al.

1971; Genest et al. 1983). The present results clearly demonstrate the clinical effectiveness of α -hANP on ischemic renal damage. It was first found that α -hANP markedly improved renal function after renovascular surgery. Although blood pressure was not changed, total peripheral resistance decreased markedly, and GFR increased. Since fractional excretions of water and sodium were not changed, the main mechanism of action of α -hANP seems to increase renal blood flow secondary to the decreased renal vascular resistance as previously reported in normal subjects and hypertensive subjects (Richards et al. 1985; Ishii et al. 1986; Weidmann et al. 1986). As implied in previous studies, α -hANP increased GFR secondary to the increased renal blood flow, though renal blood flow was not measured in this study. However, we can not exclude the possibility that α -hANP directly acted to the nephron to decrease the reabsorption of water and electrolyte because of the increased fractional phosphate excretion and the potassium clearance. Since GFR was decreased from 77.7 to 60.5 ml/min immediately after the reconstructive surgery, ischemic renal damage of the left kidney was present immediately after the surgery. However, GFR was increased to 101.2 ml/min by the infusion of α -hANP and its level was similar to the level of GFR finally obtained two weeks after surgery (96.3 ml/min). These results appear to indicate that α -hANP might act on the ischemic kidney. However, this does not of course preclude that α -hANP acted on the contralateral kidney as well as to the ischemic kidney. Anyway, α -hANP seems clinically applicable as a protective agent in renal ischemia at renovascular surgery as well as renal transplantation.

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