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Effects of Atrial Natriuretic Peptide on Systemic and Renal Hemodynamics and Renal Excretory Function in Patients with Chronic Renal Failure*

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Summary. We examined the effects of 60 min α-hANP infusion (24 ng/min/kg) on glomerular filtration rate (GFR), renal blood flow (RBF), cardiac index (CI) and blood pressure (BP) in 8 patients with chronic renal failure (CRF) with GFR ranging from 18 to 80 ml/min/1.73 m^2 and in 8 control (C) subjects with normal renal function. Basal plasma levels of ANP and cGMP were elevated in CRF (ANP: 60.6 ± 9.1 vs 13.6 ± 1.9 pmol/l, $p < 0.05$; cGMP: 14.3 ± 2.9 vs 6.6 ± 1.1 pmol/ml, $p < 0.05$). During ANP infusion, peak levels of cGMP were higher in CRF than in C (27.5 ± 3.2 vs. 17.3 ± 1.3 pmol/ml, $p < 0.05$). During ANP infusion, GFR increased in CRF by $70.7 \pm 4.2\%$ from 34.5 ± 6.8 to 57.4 ± 9.9 ml/min/1.73 m^2 ($p < 0.001$) as compared to $16.2 \pm 1.4\%$ in C ($p < 0.001$ vs CRF). RBF increased in CRF by $43.6 \pm 6.4\%$ and in C by $3.1 \pm 1.2\%$ ($p < 0.01$). Basal urinary sodium excretion ($U_{Na}V$) was slightly lower in CRF than in C but rose to the same level in both groups during ANP infusion. In CRF, as opposed to C, $U_{Na}V$ remained elevated above baseline after the end of the infusion. The effect of ANP on fractional sodium excretion (FE_{Na}), however, was more pronounced in C. Basal FE_{Na} was higher in CRF ($12.8 \pm 2.5\%$ vs $2.4 \pm 1.5\%$ in C, $p < 0.001$), FE_{Na} remained elevated at 180% over baseline in C sixty minutes after cessation of ANP infusion, while it had returned to baseline in CRF. During ANP infusion, CI increased in CRF after 30 min from 2.91 ± 0.08 to 3.12 ± 0.09 l/min/m^2 ($p < 0.001$) and in C from 3.20 ± 0.11 to 3.39 ± 0.13 l/min/m^2 ($p < 0.05$). Mean arterial BP was higher in CRF and its decrease was greater than in C ($21.1 \pm 2.7\%$ vs $9.1 \pm 1.0\%$, $p < 0.001$). In patients with CRF GFR, RPF, and CI remained significantly elevated and BP was still significantly decreased 60 min after ANP infusion. Total peripheral vascular resistance (TPR) was elevated in CRF and declined during ANP infusion in both CRF and C. The decline of TPR was sustained and more pronounced in CRF than in C. Renal vascular resistance (RVR) was high in CRF and dropped by nearly 50% during ANP infusion, whereas only a moderate decline in RVR during ANP application was observed in C. Thus, exogenous ANP had greater and prolonged effects on systemic hemodynamics and renal function in CRF than in C. They may be due to higher levels of ANP following ANP infusion and appear to be mediated by a more sustained formation of the second messenger cGMP.

Key words: ANP – Renal failure – Hemodynamics – Renal function – Sodium homeostasis – Renin-aldosterone-axis

* Dedicated to Prof. Dr. med. F. Krück on the occasion of his 70th birthday

Abbreviations: ANP = atrial natriuretic peptide; CRF = chronic renal failure; GFR = glomerular filtration rate; FF = filtration fraction; ERPF = effective renal plasma flow; ERBF = effective renal blood flow; BP = blood pressure; MAP = mean arterial blood pressure; HR = heart rate; SV = stroke volume; CO = cardiac output; CI = cardiac index; TPR = total peripheral resistance; RVR = renal vascular resistance; $U_{Na}V$ = urinary sodium excretion; FE_{Na} = fractional sodium excretion; PRA = plasma renin activity; ECFV = extracellular fluid volume; PAH = p-aminohippuric acid

The role of atrial natriuretic peptide (ANP) in extracellular fluid volume (ECFV) and electrolyte homeostasis and in blood pressure regulation is still poorly understood. In normal subjects, plasma ANP concentrations acutely increase in response to saline infusion [20, 46], water immersion [8, 18, 22], a high salt intake [9, 45] or in response to supine position [14, 17]. Furthermore, numerous

studies have demonstrated elevated plasma concentrations in a number of disease states associated with an elevation of ECFV. Thus, endogenous ANP has been shown to be increased in liver cirrhosis [7, 10, 26], congestive heart failure [4, 25], primary aldosteronism [9] and chronic renal disease [32, 35, 44].

Chronic renal failure (CRF) is usually associated with sodium retention, activation of the renin-angiotensin system and hypertension. These alterations may occur in early stages of the disease without severe fluid overload and without formation of edema. In these patients, as well as in animal models with reduced renal mass, body sodium homeostasis is still preserved by an increase in the fractional excretion of sodium (FE_{Na}). It has been proposed that ANP may play an important role in mediating this effect because the increase of FE_{Na} in CRF is abolished when sodium intake is reduced in proportion to the reduction in GFR [36, 37]. Under these conditions ANP concentrations do not increase. Substantial evidence has emerged in vivo and in vitro that ANP contributes to the adaptive changes in patients with CRF [5, 28].

ANP may modulate ECFV, sodium excretion, and blood pressure via direct effects on renal excretory function, vascular smooth muscle tone and/or via modulation of other hormonal systems such as the renin-angiotensin system and aldosterone. These multiple effects may contribute to the maintenance of body fluid and electrolyte homeostasis. In order to assess the role of ANP in CRF, exogenous ANP has been administered to patients with CRF. Depending on dose and type (bolus vs infusion) of application and selection of patients discrepant results were obtained with regard to blood pressure, renal excretory functional, and hormonal responses [2, 5, 41, 42]. In particular, little is as yet known about changes in systemic and renal hemodynamics in response to ANP and their relation to changes in renal excretory function and hormonal changes, especially of the renin-angiotensin-axis. The aim of the present study was to examine the effects of an infusion of α-hANP on systemic and renal hemodynamics, on renal excretory function, and on hormonal changes in non-edematous, non-dialyzed patients with mild to moderate CRF.

Patients and Methods

Eight non-edematous non-dialyzed patients with CRF aged 34 to 70 (mean 51.9 ± 3.4) years and eight age-matched healthy control (C) subjects (mean 54.1 ± 4.1 years) were included in this study. All subjects had given their informed written consent according to the Declaration of Helsinki. Their mean body weight was 67.4 ± 2.1 kg in CRF patients and 71.1 ± 2.7 kg in controls. To exclude overt cardiac or hepatic disease or the presence of nephrotic syndrome, a physical examination including fundoscopy, a complete hematologic and blood chemistry status, urine analysis, electrocardiogram and chest x-ray were performed in CRF patients and in controls.

The etiology of CRF was proven to be glomerulonephritis by renal biopsy in four patients. Two patients had analgetic nephropathy and two patients had CRF of unknown etiology. Renal insufficiency had been known for 2 to 10 years. Glomerular filtration rate (GFR) in CRF patients ranged from 18 to 80 ml/min/1.73 m^2 with a mean of 34 ± 7 ml/min/1.73 m^2.

Prior to the study all drugs had been discontinued for at least 10 days in all subjects. The patients had not been on a protein-restricted diet and fluid intake was also unrestricted. Their diet had a normal sodium content and their urinary sodium excretion was 182 ± 7 mmol/24 h as compared to 171 ± 19 mmol/24 h in C. Urinary potassium excretion was 96 ± 11 mmol/24 h and was not different from that in C (86 ± 16 mmol/24 h).

The following protocol was performed in an identical manner in patients with CRF and in control subjects. After an overnight fast all subjects received 15 ml of tap water per kg body weight between 6:00 and 7:00 a.m. Plastic cannulae were inserted into both antecubital veins. One port was used for infusion of inulin, p-aminohippuric acid (PAH) and for infusion of α-hANP, which was kindly provided by Drs. M. Bornemann and H. Küppers, Schwarz Pharma, Monheim, FRG. The contralateral port was used for blood sampling.

All subjects resumed supine position at 7:00 a.m. when a priming dose of inulin and PAH was administered followed by a continuous infusion of inulin and PAH in 0.9% saline to maintain constant plasma concentrations. At 8:00 a.m. two control clearance periods of 30 min each were started. They were followed by two 30 min clearance periods during which α-hANP was infused, i.e., a total of 1 h of α-hANP infusion. For this purpose α-hANP was administered intravenously at a rate of 24 ng/min/kg body weight using a calibrated infusion pump (Braun, Melsungen, FRG). The ANP infusion was again followed by two 30 min post-infusion clearance periods. During or after the infusion of α-hANP no side effects or adverse reactions were observed.

Venous blood was drawn at the end of the first

control period, after 30 min of α-hANP infusion, and again at the end of the first post-infusion clearance period. Urine was collected at the end of each clearance period by spontaneous voiding in upright position after blood samples had been collected and hemodynamic parameters had been measured. Blood pressure (BP) determined sphygmomanometrically and heart rate (HR) were measured at 10 min intervals. Stroke volume (SV) was determined by a Minnesota Impedance Cardiograph (Diefenbach, Frankfurt a.M., FRG) at the end of each 30 min urine collection period and at 10 min intervals during the α-hANP infusion period. Cardiac output (CO) was calculated automatically from the mean values of each 10 measurements of SV and is given as cardiac index. Total peripheral resistance (TPR) was calculated from mean arterial pressure (MAP) and CO: TPR = MAP/CO. Effective renal plasma flow (ERPF) and GFR were estimated from inulin and PAH clearances, respectively [6]. Renal vascular resistance (RVR) was calculated from MAP and effective renal blood flow (ERBF): RVR = MAP/ERBF; ERBF = ERPF/(1-hematocrit).

For determination of ANP plasma concentration by radioimmunoassay, 5 ml of blood were collected into chilled siliconized glass tubes containing 500 µl EDTA and were centrifuged at 4° C for 5 min at 1700 g. Extraction of α-hANP was performed with Sep-Pak C-18 cartridges as previously described with a recovery rate of 63.1 ± 4.7% [29]. Radioimmunoassay was performed as previously described using an antibody against synthetic α-hANP and ^{125}I-α-hANP was purchased from Peninsula Laboratories (St. Helens, Merseyside, England). The effective range of the standard curve for α-hANP was between 0.5 and 50 pmol per assay tube.

Plasma concentration of cyclic guanosine monophosphate (cGMP) was determined with a commercially available radioimmunoassay kit (Amersham, Braunschweig, FRG) according to the method previously described by Steiner et al. [40]. Plasma concentrations of vasopressin [13] and of aldosterone [43] and plasma renin activity (PRA) [5] were measured radioimmunologically according to methods previously described. Plasma and urinary concentrations of sodium and potassium were determined by flame photometry, and serum creatinine concentrations were determined according to a conventional autoanalyzer method. Plasma and urine concentrations of inulin and PAH were determined according to the instructions of the pharmaceutical companies. Clearances were calculated with conventional formulas.

Values of systemic and renal hemodynamics and for renal excretory function before, during, and after α-hANP infusion in each individual were calculated as means of the two respective 30 min clearance periods.

Statistical analysis was performed with Student's *t*-test, the Mann-Whitney U-test, or when appropriate with Wilcoxon's signed rank test. A $p < 0.05$ was considered to be statistically significant. Data are given as mean ± SEM.

Results

Plasma ANP and cGMP Concentrations

Basal plasma concentrations of ANP were higher in patients with CRF than in control subjects (60.6 ± 9.1 pmol/l vs 13.6 ± 1.9 pmol/l, $p < 0.001$) (Fig. 1 A). Peak concentrations of ANP during ANP infusion were also significantly higher in CRF than in C (198.4 ± 19.9 pmol/l vs 119.4 ± 7.3 pmol/l, $p < 0.001$). 60 min after the end of the infusion period ANP concentrations had declined to basal levels in C but still remained elevated in CRF (81.6 ± 13.3 pmol/l vs 14.0 ± 1.8 pmol/l, $p < 0.001$).

Basal plasma concentrations of cGMP were also higher in CRF than in C (14.3 ± 2.9 nmol/l vs 6.6 ± 1.1 nmol/l, $p < 0.001$). Peak concentrations during ANP infusion were 27.5 ± 3.2 nmol/l in CRF and thus significantly higher than in C (17.3 ± 1.3 nmol/l, $p < 0.001$) (Fig. 1 B).

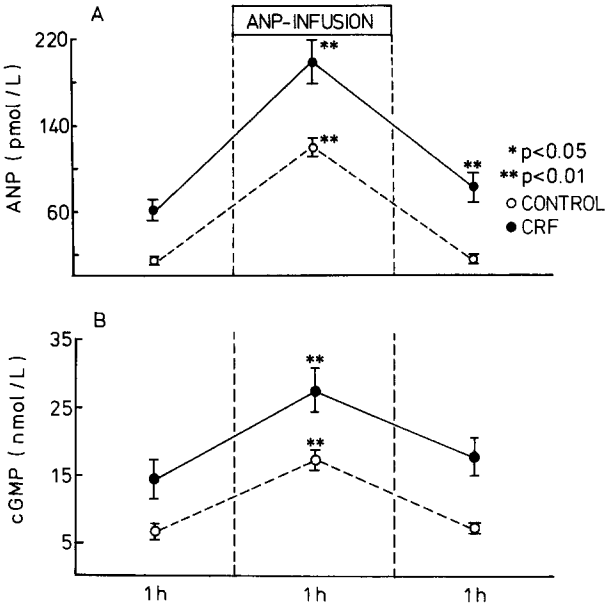

Fig. 1. ANP (A) and cGMP (B) plasma concentrations before, during, and after infusion of α-hANP

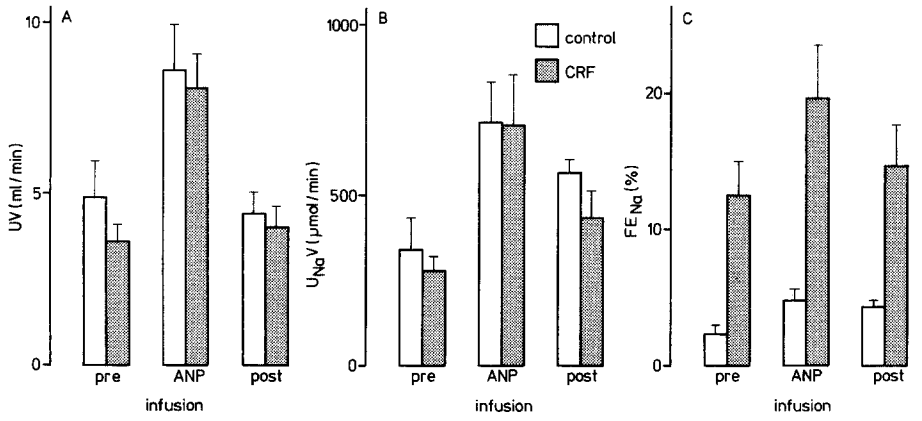

Fig. 2. Diuresis (UV, panel A), natriuresis ($U_{Na}V$, panel B), and fractional sodium excretion (FE_{Na}, panel C) before, during, and after infusion of α-hANP

Renal Function

Urinary flow rate before, during, and after ANP infusion was not significantly different between the two groups (Fig. 2A). Urinary volume increased approximately 2.5 fold in both groups during ANP infusion and returned to baseline values within 1 hr after the infusion.

In patients with CRF GFR was 34.5±6.8 and rose to 57.4±9.9 ml/min/1.73 m^2 during ANP infusion, thus showing an increase of 70%. Sixty min after ANP infusion GFR was still above basal values (44.0±9.3 ml/min/1.73 m^2, $p<0.01$ vs basal). The relative increment of GFR in the control group was smaller, increasing by 16% from 117.1±3.6 to 135.7±2.9 ml/min/1.73 m^2 ($p<0.001$) during ANP infusion; GFR declined to basal values within 1 hr after ANP infusion (Fig. 3A).

ERBF slightly but significantly increased in C during ANP application by 3% from 976±42 to 1005±39 ml/min/1.73 m^2 ($p<0.05$). In CRF patients ERBF rose by 44% from 124±38 ml/min/1.73 m^2 to 172±49 ml/min/173 m^2 and still remained elevated beyond the end of ANP infusion (Fig. 3B).

In CRF the ANP-induced absolute increments of GFR and RBF showed a large scatter due to a wide range of basal values. However, the relative increases in percent of basal values were very similar in all patients and were much greater than in the control subjects.

Filtration fraction rose moderately in both groups. Again, in CRF, as opposed to the control group, filtration fraction remained elevated after the end of ANP infusion (Fig. 3C).

Basal urinary sodium excretion was slightly lower in CRF than in C (Fig. 2B). During ANP infusion sodium excretion rose to the same level in CRF as in C and remained elevated in CRF

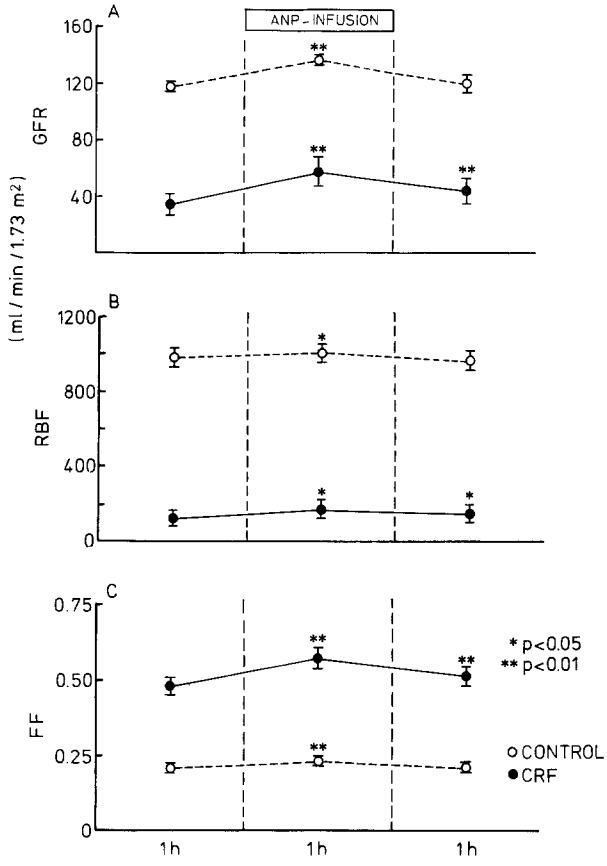

Fig. 3. Glomerular filtration rate (GFR, panel A), renal blood flow (RBF, panel B), and filtration fraction (FF, panel C) before, during, and after infusion of α-hANP

even after the end of ANP infusion. Differences between the two groups were not significant. Basal fractional sodium excretion was significantly elevated in CRF (12.74±2.54% vs 2.40±0.58% in C, $p<0.01$) and rose to 19.72±3.89% with ANP. A much smaller rise in fractional sodium excretion

Table 1. Mean arterial blood pressure (BP) and heart rate (HR) in controls and in CRF patients before, during, and after infusion of α-hANP

		ANP infusion			
	pre-	during		post-	
		30′	60′	30′	60′
Controls					
MAP (mmHg)	92.6±0.8	84.6±1.0[c]	84.2±1.1[c]	88.1±1.5[a]	93.1±1.3
HR (bpm)	72±3	74±4[a]	72±3	72±3	72±3
CRF patients					
MAP (mmHg)	128.0±3.4[d]	110.0±4.2[c]	101.3±4.7[c]	114.2±5.6[b]	123.1±4.6[a]
HR (bpm)	77±6	80±6[a]	79±6	79±6	79±6

[a] $p<0.05$ vs pre-infusion
[b] $p<0.01$ vs pre-infusion
[c] $p<0.001$ vs pre-infusion
[d] $p<0.001$ vs pre-infusion in controls

to 4.81±0.94% was observed in the control group (Fig. 2C).

Cardiovascular Parameters

Heart rate was not significantly different between patients with CRF and control subjects. In both groups there was a slight increase within the first 30 min of ANP infusion (Table 1).

Mean BP was elevated in CRF and declined by 21.2±2.7% after 60 min of ANP infusion, while in control subjects BP decreased by a maximum of 9.1±1.0% (Table 1). In CRF reduction of BP was sustained for 1 hr after ANP infusion.

Cardiac index (CI) did not differ between the two groups (Fig. 4A). There was an increase of CI during ANP infusion that was more sustained in the CRF group. Total peripheral resistance (TPR) was elevated in CRF (193.8±4.5 vs 127.7±44.0 kPa·s/l in C, $p<0.001$) (Fig. 4B). The decline of TPR with ANP infusion was sustained and much more pronounced in CRF than in C (−19±2% in CRF vs −9±1% in C after 1 hr of ANP infusion, $p<0.001$).

Renal vascular resistance was drastically elevated in CRF and dropped by nearly 50% during ANP infusion from 13532±2584 to 7368±1352 kPa·s/l ($p<0.01$). In C there was a moderate decline of RVR during ANP by 12% from 766±35 to 679±37 kPa·s/l ($p<0.001$) (Fig. 5).

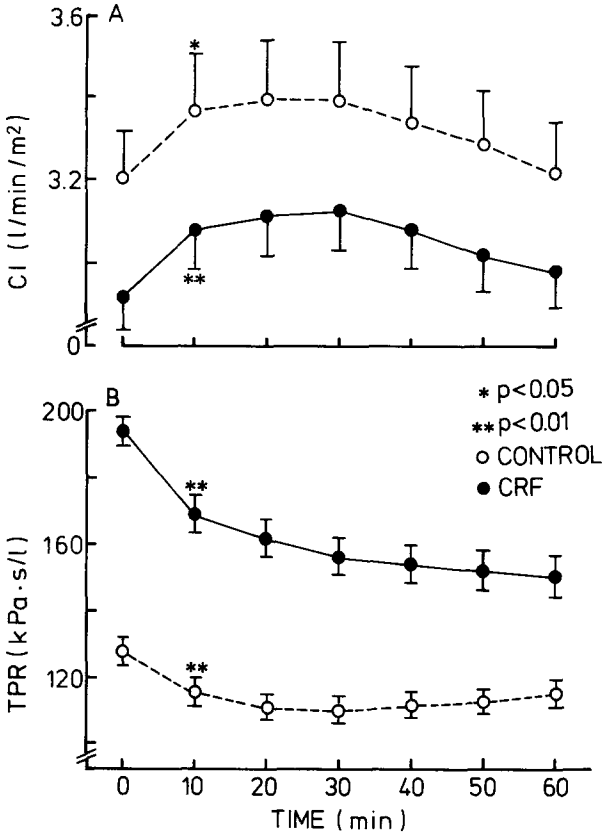

Fig. 4. Cardiac index (CI, panel A) and total peripheral resistance (TRP, panel B) before, during, and after infusion of α-hANP

Hormonal Responses

Basal plasma renin activity (PRA) was elevated in CRF, decreased during ANP infusion and reached its lowest level 60 min after the end of the ANP infusion (Table 2). In control subjects PRA declined by 30% during ANP infusion and also reached its lowest level 60 min after the infusion. The relative decrease of PRA was more pronounced in C than in CRF (−64±9% in C vs

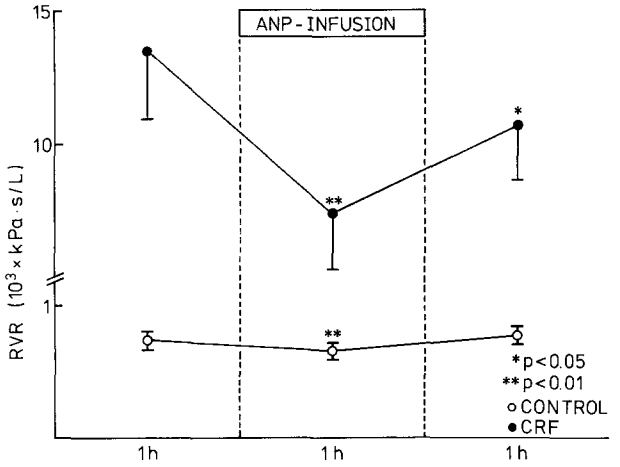

Fig. 5. Renal vascular resistance (RVR) before, during, and after infusion of α-hANP

Table 2. Effects of α-hANP infusion on plasma renin activity (PRA), plasma aldosterone concentration, and plasma concentration of vasopressin (AVP)

	PRA (ng/ml/h)	Aldosterone (ng/l)	AVP (ng/l)
Controls			
pre	0.50±0.09	104±9	1.2±0.3
during ANP infusion	0.34±0.08[a]	72±4[a]	1.4±0.2
post	0.27±0.07[c]	73±4[a]	1.8±0.3
CRF patients			
pre	1.21±0.23[d]	182±23[c]	2.1±0.6
during ANP infusion	1.02±0.21[a]	97±6[b]	2.9±0.6
post	0.77±0.16[b]	112±12[a]	3.2±0.5[a]

[a] $p<0.05$ vs pre-infusion
[b] $p<0.01$ vs pre-infusion
[c] $p<0.001$ vs pre-infusion
[d] $p<0.05$ vs pre-infusion in controls
[e] $p<0.01$ vs pre-infusion in controls

$-41\pm7\%$ in CRF, 60 min after ANP infusion, $p<0.01$).

Basal plasma aldosterone levels were increased in CRF (Table 2), declined by 41% during ANP infusion and increased slightly again within 60 min after infusion. In controls plasma aldosterone concentrations initially fell by 26% as compared to the pre-infusion level, but this effect was sustained until 60 min after the end of ANP infusion.

Plasma concentrations of vasopressin (AVP) were higher in CRF (Table 2), increased moderately during infusion of ANP and reached maximal concentrations 60 min after the end of the infusion. In controls no significant increase in AVP plasma concentrations was observed.

Discussion

Elevated plasma concentrations of ANP have been implicated in the adaptive changes of renal excretory function in patients with CRF [28]. While administration of exogenous ANP in healthy subjects almost unequivocally induced diuresis and natriuresis, the hemodynamic effects and the mechanisms of action of ANP in CRF are still a matter of debate.

The data from the present study confirm previous studies reporting elevated endogenous plasma ANP concentrations in patients with CRF [3, 5, 27, 41, 44]. Although the kidneys are one of the clearance sites for ANP, it is rather unlikely that the decrease of GFR alone accounts entirely for the rise in plasma ANP [24, 47]; plasma half-life prolongation of exogenous ANP in endstage renal disease has been shown to be only 30% [42]. This is in accordance with recent evidence that other organs than the kidney substantially contribute to the clearance of ANP [12]. Administration of ANP increased ANP concentrations almost tenfold in controls and approximately threefold in patients with CRF. These changes were paralleled by an increase in plasma cGMP concentrations.

The present results strongly indicate a major effect of ANP on vascular resistance and cardiac output. ANP infusion induced a decline in BP in both the control and the CRF group. Patients with CRF had mild arterial hypertension under control conditions. The drop in BP during ANP infusion was much more pronounced in this group than in the healthy controls. In association with elevated BP peripheral vascular resistance was found to be significantly higher in CRF. It dropped with ANP infusion in both groups, but again, the response was greater in the CRF group. The drop in vascular resistance was associated with an increase in cardiac output.

As expected, renal vascular resistance was high in patients with CRF. In these patients renal vascular resistance dropped by 45% as compared to only 12% in the control group. These data are in support of previous observations that the vasodilatory action of ANP is positively correlated to the preexisting vascular tone [33]. In the present study we did not observe a significant rise in hematocrit during ANP infusion as it has been reported by others [41, 42]. Although our experimental data do not exclude a shift of fluid into the extracellular space, the major mechanism of ANP to lower BP in the present study clearly appears to be vasodilation.

Consistent with the finding of reduced systemic and renal vascular resistance is the increase in RBF

observed during ANP infusion. GFR also increased in both groups with ANP infusion, the relative increase compared to basal values was significantly greater in patients with CRF. According to the greater increase of GFR as compared to ERBF, filtration fraction (FF) increased in both groups.

While these data are in accordance with our previous findings in diabetic patients [30], results from the literature regarding the effects of exogenous ANP on GFR, RBF, and FF are inconsistent. In healthy subjects a low-dose infusion of ANP did not affect BP and heart rate [34, 38] or GFR [34]. In another study in patients with mild to moderate renal failure using ANP doses comparable to those in the present study, BP was reduced and GFR was slightly increased resulting in a rise in FF [41]. In patients with end-stage renal disease on dialysis, BP and heart rate remained unchanged during a one hour ANP infusion at 10 pmol/kg/min [42]. These latter findings, however, have to be appreciated in the view of the presence of virtually non-filtering kidneys. On the other hand, acute systemic and renal hemodynamic changes have been observed with higher doses of ANP applied as either continuous infusion [45] or as bolus [2]. The dose of ANP used in the present study, although comparably low, may well have activated cardiovascular counterregulatory mechanisms as may be concluded from a drop in BP and a slight increase in heart rate.

Diuresis was stimulated by ANP to the same degree in both groups. Also, absolute sodium excretion was slightly but not significantly higher in the control group than in the patients with CRF. The effect of ANP on fractional sodium excretion (FE_{Na}), however, was more pronounced in C. Basal FE_{Na} was higher in CRF ($12.8 \pm 2.5\%$ vs $2.4 \pm 1.5\%$ in C, $p < 0.001$), but in C, FE_{Na} remained elevated at 180% over baseline 60 min after cessation of ANP infusion, while it had returned to pre-infusion levels in CRF. Increased FE_{Na} in CRF patients under basal conditions as well as during ANP infusion quite obviously accounts for the ability to maintain sodium balance in advanced renal failure. The present findings are consistent with results by others in healthy subjects [38] as well as in patients with CRF [41]. The rise in FE_{Na} indicates that GFR is not the only determinant of ANP-induced natriuresis. Since we found a significant increase in RBF, alterations of the peritubular Starling forces may contribute to the natriuretic effect of ANP possibly via medullary wash-out [21, 31] resulting from intrarenal blood flow redistribution towards the renal medulla [1]. Other intrarenal mechanisms that may be involved in the natriuretic effect of ANP may include direct proximal [15, 16] or distal [39] tubular effects. These GFR-independent effects of ANP on renal sodium excretion appeared to be more pronounced in healthy subjects than in patients with CRF.

Effects of ANP on the renin-angiotensin-aldosterone axis may also contribute to changes in renal excretory function. Basal PRA and plasma aldosterone concentrations were both increased in the CRF group, declined during ANP infusion and reached their lowest level 60 min after cessation of the ANP infusion. These findings are in accordance with other studies in healthy subjects and in diabetic patients [30, 33, 45]. However, others did not observe a decline of either PRA or plasma aldosterone during ANP administration in chronic renal failure; rather, they found an increase in both plasma renin activity and aldosterone in the recovery phase [41]. The authors hypothesize that the drop in BP and the rise in hematocrit may counterbalance the inhibitory effect of ANP on renin release. No changes in PRA were observed with ANP infusion in patients with end-stage renal disease on dialysis [42]. This may indicate that a certain amount of filtered fluid and sodium, respectively, is needed to mediate renin inhibition at the juxtaglomerular apparatus. The increase of plasma AVP concentrations that was observed only in CRF patients during ANP infusion may reflect the activation of vasopressor systems in response to the hemodynamic changes that had been more pronounced in the CRF group.

The present study demonstrates a profound effect of exogenous ANP on hemodynamics and renal excretory function in patients with CRF. In particular, ANP reduced BP, increased cardiac output, and drastically reduced systemic and renal vascular resistance. The pronounced and prolonged effect of ANP in CRF may in part be due to a decrease in ANP and/or cGMP clearance. Furthermore, the systemic and renal vasculature reveals a higher sensitivity to the vasodilatory effect of ANP in CRF. This may be attributable to the presence of an enhanced activity of vasopressor and sodium retaining systems rendering the vasculature more susceptible to the effects of ANP. On the other hand, the renal excretory response to ANP in terms of FE_{Na} appeared to be blunted in patients with CRF. In various animal models it has been shown that ANP receptor status may be altered in response to changes in sodium balance [11, 19, 23]. It is, therefore, conceivable that these mechanisms play an important role in the alterations of the cardiovascular and the renal excre-

tory response to ANP in CRF. This issue clearly awaits further investigation.

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Buchbesprechung

Die Verlage werden gebeten, von der unverlangten Zusendung von Besprechungsexemplaren abzusehen und zunächst eine Anfrage an die Redaktion zu richten, die gegebenenfalls dann ein Exemplar erbitten wird. Für die Rückgabe unverlangt eingesandter Besprechungsexemplare kann keinerlei Gewähr übernommen werden.

G. Dagnini: **Laparoscopy and Imaging Techniques.** 206 Seiten, 187 Abbildungen, davon 150 in Farbe, 17 Tab. Springer, Berlin Heidelberg New York Tokio Hong Kong 1990. Hardcover DM 298,– (ISBN 3-540-50999-2)

In einer Zeit der stürmischen Entwicklung laparoskopischer Operationen und laparoskopischer Eingriffe bei internistischen Krankheitsbildern wird dieses Buch eines erfahrenen Laparoskopikers vorgelegt.

Es ist in 2 große Kapitel eingeteilt: 1. Fortschritte in der Laparoskopie; 2. gegenwärtige Anwendungen der Laparoskopie.

Im 1. Kapitel werden nach der Darstellung neuer Instrumente und technischer Verbesserungen auch Vergleiche mit anderen bildgebenden Verfahren wie der Sonographie ausführlich abgehandelt. Dabei kommt der Autor zu dem erfreulichen Entschluß, daß die Sonographie als ein „Filter" dient, um die Anzahl unnötiger oder sinnloser Laparoskopien auf ein Minimum zu reduzieren. In dem Abschnitt technischer Erneuerungen werden auch laparoskopische Operationen beschrieben sowie Biopsien von Leber, Pankreas und Milz ausführlich dargestellt.

Der Schwerpunkt des Buches befaßt sich aber mit traditionellen Indikationen für die Laparoskopie. Nach entsprechender Darstellung der typischen gastroenterologischen Krankheitsbilder erfolgt immer eine präzise Zusammenfassung der derzeitigen Indikation für eine Laparoskopie.

Am Ende eines jeden Kapitels wird in einer Zusammenfassung, die sich auch bildlich vom übrigen Text abhebt, das Wichtigste in 3 prägnanten Sätzen konzentriert. Zwei große Abschnitte befassen sich mit den Erkrankungen der Leber und der Laparoskopie in der Onkologie. Das letzte Kapitel zeigt die Möglichkeiten der Laparoskopie in Notfallsituationen sowohl bei einem akuten Abdomen als auch bei abdominellen Traumen. Das Buch zeichnet eine klare Gliederung mit Zusammenfassungen, übersichtlichen Tabellen und einem aktuellen Literaturverzeichnis aus.

Das Bildmaterial ist in allen Kapiteln hervorragend und zeigt nicht nur bisher bekannte laparoskopische Befunde, sondern auch ausgewählte Raritäten.

Es macht Freude, dieses Buch zu lesen. Bei der ausführlichen Darstellung aller gastroenterologischen Erkrankungen und der darüber hinausgehenden Beschreibung endoskopischer Operationen wird dieses Buch gleichermaßen in Gastroenterologenkreisen wie auch bei den chirurgischen Kollegen auf größtes Interesse stoßen.

Der Preis von DM 298,– ist hoch, bei der ausgezeichneten Qualität des farbigen Bildmaterials und des Hochglanzpapieres sicherlich gerechtfertigt. W.G. Zoller (München)