ANGIOTENSIN-CONVERTING ENZYME IN PATIENTS WITH CHRONIC RENAL FAILURE ON HEMODIALYSIS

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The serum angiotensin-converting enzyme (ACE) plays an important role in regulation of circulating vasoactive peptides. ACE realizes the interrelation between kinin and renin-angiotensin system (RAS) by means of converting angiotensin —I into angiotensin —II and of simultaneous inactivation of the hypotensive bradykinin (1,4).

A number of authors confirmed its importance for the diagnostics and treatment of sarcoidosis (11). ACE diagnostic significance in various kinds of pulmonary, skin, heart, and liver diseases was also discussed (7, 8, 10, 13). Recently, treatment of severe hypertension which is hard to be well in hand was directed towards ACE-inhibiting drugs (1). ACE intrarenal secretion, its high tubular epitheloid cells' concentration, its impossibility to pass through the intact glomerule as well as the attempt to find a manner of treating severe, even dialysis-resistent hypertension asks a question of its diagnostical importance in chronic renal failure (CRF) patients (12). Having in mind the possibilities for altering the lung epitheloid cells during hemodialysis (HD) and the related disturbances of kinin, fibrinolytic, complement, and renin-angiotensin systems (2, 3, 4, 5, 9, 12), we had the aim to study ACE changes in CRF patients on chronic HD.

Material and methods

ACE level was studied in a total of 84 individuals divided into 3 groups: 1st — 24 CRF patients (19 males and 5 females) aged between 20 and 54 years on maintenance HD for 3 till 94 months long twice-thrice weekly with total duration of 12—15 hours by using the dialysator capillary type "CORDIS" (USA). Blood pressure 26,6—15,3/15,96—7,98 kPa, at the average 19,42 (11,17 kPa; IInd — 6 CRF patients (3 males and 3 females) aged between 30 and 56 years on conservative therapy; IIIrd — 54 clinically healthy blood donors (30 males and 24 females) aged between 20 and 50 years.

The serum ACE was determined spectrophotometrically according to Cushmas et Cheung's method (6) by using as substrate hippuril, histidyl, leucine — SERVA (GFR). It was estimated in nmol/ml/min. Blood samples were taken in the morning before meal at 0 °C. It was done in HD patients before and after HD by using venous puncture of the arteriovenous fistula. HD patients' renin activity was determined in ng/ml/h by means of a radioimmunological method with test package from the firm "Rotop" (GDR).

The results obtained were processed statistically according to the method of variation analysis and presented on tables.

Results and discussion

ACE level didn't change statistically significantly in CRF patients both on HD (20,16±7,16) and without HD (18,37±8,55) as compared with that of the controls (19,57±6,88) ($p > 0,05$) (see table 1). The dialysis procedure didn't cause

Table 1

ACE in CRF patients on HD and concervative treatment in nmol/ml/min

	Healthy	CRF Patients		
		without dialysis	on hemodialysis	
			before HD	after HD
$\bar{x}$	19,57	18,73	20,16	23,26
S	6,88	8,55	7,16	12,05
Sx	0,93	3,82	1,46	2,40

any statistically reliable changes of ACE values (from 20,16±7,16 before HD till 23,28±12,05 after HD) ($p > 0,05$) (table 1). This tendency towards ACE increase immediately after HD (table 1) is clarified after separation of certain HD patients with ACE values exceeding $\bar{x}+2S$ (table 2 and 3) at the end of HD. From

Table 2

ACE in a group of 6 males with CRF on chronic HD according to $\bar{x}$ and 2S rates in nmol/ml/min after HD

	Healthy (males) n—30	CRF Patients on HD	
		before HD	after HD
		n—6	
$\bar{x}$	19,63	28,26	39,98
S	6,17	4,10	4,79
Sx	1,12	1,82	2,13

this point of view it is to be noted that these patients show significant ACE changes ($p < 0,05$) at the end of HD and even before it as compared with the controls and CRF patients.

A comparison is made with a collected control group (both males and females) as well as with a control group of 30 healthy blood donors (males). There is no relation between ACE changes, on the one hand, and age, blood pressure, and HD duration, on the other. The assessment of renin did not reveal any significant changes at the end of HD both in the collected group of dialysed patients (2,52± ±0,36 before HD; 2,18±0,48 after HD) ($p > 0,05$) and in the separated one (with higher ACE level (3,84±1,30 before HD and 1,98±0,55 after HD) ($p > 0,05$).

ACE level in HD patients was studied in a generalized group of CRF patients (on HD and conservative treatment) by R. Patel et al. (12) who could not establish any significant ACE changes in these patients as compared with those of the controls. However, they found out a statistically reliable ACE difference in HD

Table 3

Age, blood pressure and HD duration differences in 6 males with ACE levels over $\bar{x} + 2S$ after HD

Patient	Age (years)	Systolic blood pressure kPa		Dialysis duration (months)	Diagnosis
		beginning	ending		
N. I.	40	21,71	13,30	7	glomerulo-nephritis
P. D.	50	21,23	13,30	22	pyelonephritis
Y. U.	37	17,29	15,96	19	polycystic disease
G. B.	51	17,29	17,29	94	gout neph-ritis
E. P.	37	17,29	17,29	75	glomerulo-nephritis
I. G.	39	21,28	18,02	14	"

patients correlating with HD duration. Our results do not demonstrate such a correlation (table 3). In contrast to R. Patel's et al. data we establish a distinct ACE increase in 25 per cent of the patients at the end of HD ($p < 0,05$ — table 2) and after repeated HD as compared with that of the healthy controls.

According to some recent results (3, 5), lung endothelial cells are damaged during HD procedure. Having in mind the enzyme localization in them (7, 8) ACE increase after HD could be due to these changes in 25 per cent of the patients. The reaction of some patients as proved by R. Patel et al. can't exclude patients' individual response against HD-induced hemostatic disturbances and the different degree of complement activation followed by leukocyte microembolism (3). HD-induced disbalance in RAS, kinin-kallikrein, and fibrinolytic systems confirms our previous investigations (2). HD-induced ACE increase can be directly related to the increase of the total proteolytic activity following the decrease of some inhibitors of these systems (2). Our results support the lack of correlation between renin and blood pressure in HD patients reported by D. Koev et al. (4) on the one hand, and, between ACE, blood pressure, hematocrit, and age according to R. Patel et al. (12), on the other.

It is obvious that the problem is very complicated and requires further investigations.

We can conclude that ACE changes in CRF patients on HD and conservative treatment are insignificant in comparison with these of healthy controls ($p > 0,05$). In 25 per cent of HD patients there is, however, a statistically reliable ACE increase after HD ($p < 0,05$). There is not any correlation between ACE changes, HD duration, patients' age, blood pressure and renin.

REFERENCES

1. Беловеждов, Н. *Вътр. болести*, 1981, № 6, 30—34. 2. Янкова, Т., П. Чанкова, Д. Ненов. В: Нац. конгр. вътр. болести, VII. Плевен, 1982, с. 63. 3. Bischel, M. D., F. L. Orrelle, et al. *Trans.*, 19. 1973, 492—497. 4. Caldwell, M. D., H. J. Wigger, et al. *Amer. J. Pathol.*, 105, 1981, 54 63. 5. Craddock, P. R., F. Fehr, et al. *N. Engl. J. Med.*, 296, 1977, 769—774. 6. Cushmas, D. W.,

H. S. Cheung. *Biochem. Pharmacol.*, 20, 1971, 1637—1648. 7. Fourrier, M. D., et al. *Chest*, 1983, 493—496. 8. Hollinger, A. M., P. A. Davis. *Chest*, 1983, No. 4, 589—590. 9. Koev, D., D. Nenov, G. Tauschanova. *Sc, Sci. Med.*, 16, 1979, 73—78. 10. Lieberman, J. *Amer. J. Med.*, 59, 1975, 365—372. 11. Lieberman, J., et al. *Ann. Intern. Med.*, 93, 1980, No. 6, 825—826. 12. Patel, R., A. Ansari, et al. *Dialys. Transplant.*, 10, 1981, No. 12, 1001—1005. 13. Raff, M., H. Bardach, M. Müller. *Arch. Dermatol. Res.*, 270, 1981, 341—345.

АНГИОТЕНЗИН-КОНВЕРТИНГ ЭНЗИМ У БОЛЬНЫХ ХРОНИЧЕСКОЙ ПОЧЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ, ЛЕЧИВШИХСЯ МЕТОДОМ ГЕМОДИАЛИЗА

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РЕЗЮМЕ

Уровень ангиотензин-конвертинг энзима исследовался спектрофотометрическим методом Cushmas u Cheung.

Проведено исследование 84 больных, которые были распределены в три подгруппы: I группа — больных хронической почечной недостаточностью, лечившихся гемодиализом; II группа — больных хронической почечной недостаточностью, лечившихся консервативно; III группа (контрольная) — клинически здоровых лиц. Не было установлено статистически значимых различий уровня ангиотензинконвертинг энзима у больных хронической почечной недостатачностью на гемодиализе и у тех, которые лечились консервативно, по сравнению с контрольной группой клинически здоровых лиц. Статистически значимое повышение количества ангиотензин-конвертинг энзима после проведенного гемодиализа наблюдалось у 25 % больных, лечившихся этим методом. Полученные результаты не дают оснований установить регулярную связь между изменениями ангиотензин-конвертинг энзима, продолжительностью хронического диализа, возрастом больных, уровнем кровяного давления и количеством ренина.