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KALLIKREIN-KININ SYSTEM (KKS) AND ANGIOTENSIN CONVERTING ENZYME ACTIVITY (ACE) IN PATIENTS ON PERIODIC HAEMODIALYSIS (PHD) TREATED WITH RECOMBINANT HUMAN ERYTHROPOIETIN (rhEPO)

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Arterial hypertension (AH) is a common problem during the treatment of patients with renal anaemia, on periodic haemodialysis treated with recombinat human erythropoetin. There is so far no explanation for this.We decided, along with a clinical trial of rhEPO (Boehringer-Mannheim), to investigate the level of some parameters which are known to take part in the regulation of blood pressure, namely: plasma activity of angiotensin-converting enzyme ACE) and kallikrein-kinin system (KKS). A total of 22 patients with CRF treated with PHD were investigated: 11 controls and 11 treated with rhEPO. All of them, aged above 18 years, had hematocrit below 28%, and PHD duration over six months. rhEPO administration was subcutaneous, 3 times a week, 10 min before the beginning of every haemodialysis treatment, with initial dosage of 20 U/kg body weight. The dose was increased, if after 6 weeks the target hematocrit of 30-35 vol% was not acchieved.Plasma ACE activity was determined spectrophotometrically after Chushman and Cheung (1971) and Liebermann (1975), modified by Chankova (1987), with Bz-Gly-His-Leu as a substrate being used. KKS activity was determined after J. Vitt at al. (1978). Student's test was used for statistical evaluations.

Table 1. Changes of plasma angiotensin-converting enzyme activity in patients on PHD and on rhEPO treatment (U/l) (p - NS)

	Patients on PHD without rhEPO			Patients on PHD and rhEPO treatment		
n	11	11	8	10	10	9
	Before treatment	After 6 months	After 12 months	Before treatment	After 6 months	After 12 months
X	25.8	27.9	22.2	28.3	24.1	22.7
SD	±13.0	± 11.0	± 4.5	± 12.1	± 7.4	9.8

The table 1 shows activity of ACE in the two groups patients on PHD-controls and treated with rhEPO. The difference between ACE activity in the two groups of patients is not significant. These results show, too, that the alterations are due to haemodialysis per se, while rhEPO treatment does not alter ACE activity. The results of KKS investigation show significant increase both of plasma prekallikrein (table 2) and kallikrein (table 3), in both groups of patients.

Table 2. Plasma prekallikrein in patients on PHD and rhEPO treatment (U/l) (* $p < 0,05$)

	Treated with rhEPO			Without rhEPO treatment		
	Before treatment	After 6 months	After 12 months	Before treatment	After 6 months	After 12 months
x	268	439	315	258	471	374
SD	± 93	± 107*	± 79	± 96	± 202*	± 135

Table 3. Plasma kallikrein in patients on PHD and rhEPO treatment (U/l) ($p < 0,05$)

	Treated with rhEPO			Without rhEPO treatment		
	Before treatment	After 6 months	After 12 months	Before treatment	After 6 months	After 12 months
x	54	161	182	39	196	161
SD	± 43	± 62	± 103	± 47	± 105	± 73

These alternations should again be explained by the haemodialysis treatment, because they are found both in the control group of p patients on PHD, as well as in those, treated with rhEPO. We relate the activation of ACE and KKS to the extracorporeal blood purification, including the remaining blood in the dialysis filters and their double and triple reuse. We conclude that: 1. The treatment with rhEPO does not change the plasma ACE activity. 2. Plasma prekallikrein and kallikrein are activated in patients on PHD. No significant difference is observed between treated and non-treated with rhEPO.