PLASMA THROMBOCYTOPOIETIN ACTIVITY IN CHRONIC RENAL FAILURE PATIENTS ON HEMODIALYSIS AND HEMOPERFUSION

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It is well known that hemostatic disorders are a common feature in chronic renal failure (CRF) patients. Thrombocyte functions are most often affected — the aggregation and adhesiveness are suppressed and thrombocyte factor 3 liberation diminishes. Thrombocyte count alters more rarely (1). The aforementioned aspects of the problem are analysed in the literature available. However, the role and importance of thrombocytopoietin (TP) — a basic humoral regulator of thrombocyte homeostasis (4) were not yet discussed. This interest is supported by the fact that kidney plays an important role in thrombocytopoietin forming mechanisms (4).

The aim of the present study is to determine plasma TP activity (TPA) in CRF patients set on periodic hemodialysis (HD) before and after both HD and hemoperfusion (HP) and to compare it with that of healthy individuals and CRF patients without HD treatment. The data obtained could enlighten the role of TP in the mechanisms of normal hemostasis restitution and maintenance of an adequate thrombocyte level in CRF patients on periodic HD (PHD).

Material and method

The trial covered a total of 17 individuals as followed: 12 CRF patients on PHD, 2 ones on HP/HD, 2 ones with CRF without HD treatment, and 3 healthy persons (controls). Patient's blood was sterilly taken before and immediately after HD. It was done in the morning on an empty stomach by using anticoagulant (heparin) when the other individuals were concerned. Separated plasma was frozen until its testing. TPA testing was performed by using of 188 white male mice-recipients after Penington's (1970) routine biological isotope method (6). The changes of ^{75}Se methionine incorporation in newly formed thrombocytes of test-mice under the influence of the examined plasma was tested. The data received were processed by use of variation statistic methods.

Results and discussion

The results were presented on table 1. The analysis of the data showed that CRF patients on PHD could be divided into two groups. The first one was characterized with a higher initial TPA — $5,80 \pm 0,46$ as compared with that of the controls that is statistically unreliable. It is an interesting fact that after HD plasma TPA reduces significantly in these patients ($p < 0,001$). Initial plasma TPA levels differ statistically significantly in the two patients' groups on PHD with an increased and a decreased TPA after PHD ($p < 0.001$).

Therefore, HD causes a significant plasma TPA increase in CRF patients on PHD with lower initial levels and a significant plasma TPA decrease in those with higher ones in comparison with that of the controls. After a combined HP/HD treatment plasma TPA is significantly reduced ($p<0,001$). The comparison of initial plasma TPA levels of all patients' groups with the control ones presents a real interest (see table 1). The initial TPA is lower in patients on PHD reacting with a TPA increase after HD, in CRF patients without HD treatment as well as in those with a combined HP/HD one which is statistically insignificant. Only the initial plasma TPA in patients on PHD which then decreases after HD is higher than that of the controls.

Table 1

^{75}Selenomethionine incorporation in newly-formed mice thrombocytes under the influence of plasma from CRF patients on PHD with HP/HD and without HD

Statistical indexes	Controls	Patients with chronic renal failure							
		Without HD	On PHD with TP increase		On PHD with TP decrease		Patients on HP/HD	
			before	after	before	after	before	after
$\bar{x}$	**4,75**	3,34	2,37	4,45	5,80	1,80	3,93	1,53
$S\bar{x}$	0,46	0,51	0,30	0,27	0,46	0,16	0,49	0,24
	$p>0,10$		$p<0,001$		$p<0,001$		$p<0,001$	

There is a tendency towards lower plasma TP levels in most CRF patients as compared with that of the healthy controls. It is very difficult to interpret these results because of the lack of similar investigations and the participation of many factors related with TP biogenesis regulation in normal conditions and CRF patients. The fact that HD corrects considerably the hemostatic disorders in these patients is indirectly confirmed by our own findings for a significant plasma TPA increase after HD in almost 2/3 of the patients on PHD. Plasma TPA increase presents a precondition for more effective and qualitative thrombocytopoiesis because, as already mentioned (7), thrombocyte functions are essentially disturbed in those patients. It is obvious that HD procedure eliminates certain inhibitors or toxic substances from the plasma of these patients. Probably, they are uraemic toxins which thrombocytopoietic inhibitory effect is already known (2). This tendency towards higher TPA after HD than the initial one is established in one female patient at the 12th hour after HD. A similar plasma erythropoietin increase after HD in CRF patients has been already found out in our previous investigation (2).

That very presence of an increased TPA in most patients on PHD can be probably the reason for more seldom thrombocytopenia and most often normal thrombocyte count.

The explanation of plasma TPA reduction in 1/3 of the patients on PHD (with high initial activity) is difficult, too. It is a point to note the statistically reliably higher initial plasma TPA than the control one in these patients ($p<0,001$). It is probable that certain plasma components which are required for demonstrating TPA are washed away, or that some ones remain in the plasma to inhibit this

activity. This speculative explanation is partially supported by J. Stewart et al. (7), and, especially, by T. Christopher, et al. (3) who report that low molecular components retention in plasma after HD is the factor partially improving hemostatic disorders and thrombocyte functions. The definitive clearance of the mechanisms giving rise to these differences and changes requires a parallel follow-up of the dynamics of thrombocyte count, the changes of the megakaryocyte line, etc.

The considerable TPA reduction after HP/HD combination by 61,07 per cent ($p < 0{,}001$) gives an evidence that some substances necessary for plasma TPA demonstration probably remain in plasma or move away in these cases, too. Most likely, HP which leads to sorption of higher-molecular substances and to a better expressed well-known transitory thrombocytopenia helps additionally to this phenomenon.

It can be concluded that plasma TPA increases in 2/3 and decreases in 1/3 of CRF patients on PHD. HD increases significantly the low initial plasma TPA but decreases more considerably the high one. There is a trend toward lower TPA in CRF patients in comparison with that of healthy individuals. HP/HD combination reduces significantly plasma TPA.

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ТРОМБОЦИТОПОЭТИНОВАЯ АКТИВНОСТЬ ПЛАЗМЫ У БОЛЬНЫХ ХРОНИЧЕСКОЙ ПОЧЕЧНОЙ НЕДОСТАТОЧНОСТЬЮ, ЛЕЧИВШИХСЯ МЕТОДАМИ ГЕМОДИАЛИЗА И ГЕМОПЕРФУЗИИ

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РЕЗЮМЕ

Исследована тромбоцитопоэтиновая активность с помощью биологического метода — тестирования плазмы больных хронической почечной недостаточностью, лечившихся консервативно методами гемодиализа и гемоперфузии. Активность определялась посредством процентного включения ^{75}-селенометионина в новообразующиеся тромбоциты самцов белых крыс.

Авторами впервые установлено повышение тромбоцитопоэтиновой активности у 2/3 больных на периодическом гемодиализе, а у 1/3 больных — понижение. Понижение тромбоцитопоэтиновой активности у больных последней группы авторы связывают с диализированием тромбоцитопоэтина или веществ, необходимых для проявления плазменной тромбоцитопоэтиновой активности. Комбинированное лечение методами гемодиализа и гемоперфузии понижает тромбоцитопоэтиновую активность.