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Abnormalities of seric profile of Lipids in Essential Hypertension with positive microalbuminuria

Introduction

Recently, the evaluation of Microalbuminuria (MA) in Essential Hypertension (EH) has caused a great interest, because this abnormality is a strong predictor of cardiovascular morbidity and mortality (1,2). MA is defined as the abnormal urinary excretion of 30-300 mg/day albumin (or 20-200 µg/min).

These levels of urinary albumin cannot be measured by conventional ordinary tests, but more accurate methods are nowadays used in clinical practice (ELISA, RIA, Nephelometry).

The prevelence of MA in EH varies widely in different studies. This variability depends on different techniques used for the detection of MA as well as on the criteria chosen for patients selection (1,3).

Why does occur that hypertensive patients with MA have an increased rise of cardiovascular diseases? Different studies in hypertensice patients with positive micro-albuminuria, attributed this increased risk to some factors such as: higher levels of Arterial Hypertension and alteration of 24 hours profile of Arterial Hypertension, resistance to insulin and increased sensitivity to salt, systemic endothelial dysfunction, increased activity of renin-angiotensis system and lastrly, the atherogenic profile of seric lipids.

The Object if this work is the study of possible existing links between MA and altered seric profile of lipids in patients with EH.

Subjects and Methods

24 patients with EH have been studied. Their mean age was 51.9+/-10.3 years. Among them, 15 patients were males and 9 females. (M:F = 15:9).

Patients with different renal and systemic diseases were excluded from the study. 16 patients were taken as control group. They had no high Blood Pressure, renal or systemic diseases, but suffered from digestive, pulmonary or allergic diseases. Their mean age was 47.5 +/-16.4 years. The sex ratio was M:F=10:6.

Table 1 - Presentation of groups according to age.

		Age (years)	P
	Cases	X ± σ	
HTA	24	51.9 ± 10.3	n.s
Group of control	16	47.5 ± 16.4	

As you can see from Table 1, no significant differences existed on the mean age between the two groups of patients.

The search for MA was made in all the patients by Micral Test (Boehringer - Manheim). The test was considered positive for MA when albuminuria was found in

the range of 30-200 mg/l. The test was repeated three times, but never in the same day. Based on the positivity of this test for MA, patients with EH were divided in two subgroups:

a)patients with EH and Positive test for MA, and

b)patients with EH and Negative test for MA.

We also measured the seric profile of Lipids by precising the different fractions of lipids in all the groups. So, it was made possible to evaluate and compare the seric levels of cholesterol, tryglicerides, phospholipides, HDL -c and LDL-c.

The evaluation of mean levels of these parameters was made using the Student Test, considering the differences significant when $p<0,05$.

Results

The study of MA in patients with EH showed positive results in 13 cases (54,2%), while in the control group MA was positive only in 2 cases (12,5%). There is a significant difference between the two groups ($p<0,01$). Table 2.

Table 2 - The prevalence of microalbuminuria in studied groups

	Cases	Nr.	%	P
HTA	24	13	54.2	p < 0.01
Group of control	16	2	12.5	

The study of seric total cholesterol levels in our patients resulted as follows: seric cholesterol levels in patients with EH were higher compared to those of the control group, but the difference was not significant. Whereas, the mean cholesterol level in patients with EH and positive MA was higher than that of patients with EH and negative MA. Again, there was not a significant difference. The difference between cholesterol levels of patients with EH and positive MA and control groups was also not significant. Table 3.

Table 3 - Cholesterolemia according to hypertension and microalbuminuria

	Colesterolemia mg.%				P
	Cases	$\bar{x}$	±	σ	
Gr. of control	16	178.75	±	38.17	n.s. n.s.
HTA	24	195.41	±	46.83	
HTA (microalb +)	13	206.76	±	59.14	n.s.
HTA (microalb -)	11	182.0	±	21.95	

A similar picture emerged when tryglicerides and phospholipides seric levels were confronted between different study groups. Table 4, 5.

Table 4 - The level of tryglicerides on the same groups.

	Tryglicerides mg. %				P
	Cases	$\bar{x}$	±	σ	
Gr. of control	16	151.37	±	78.49	n.s. n.s.
HTA	24	162.7	±	67.28	
HTA (microalb +)	13	162.38	±	38.46	n.s.
HTA (microalb -)	11	162.72	±	50.78	

Table 5 - The level of phospholipides on different groups

	Fosfolipides				P
	Cases	$\bar{x}$	±	σ	
Gr. of control	16	193.56	±	38.09	n.s n.s.
HTA	24	210.65	±	46.7	
HTA (microalb +)	13	221.76	±	59.14	n.s.
HTA (microalb -)	11	197.0	±	17.88	

The comparison of HDL-c levels pointed out another interesting picture. Table 6.

Table 6 - The level of HDL-C according to different groups

	HDL - C				P
		$\bar{x}$	±	σ	
	16	61.43	±	17.17	n.s. p < 0.05
HTA	24	54.37	±	10.71	
HTA (microalb +)	13	47.83	±	9.27	p<0.05
HTA (microalb -)	11	61.18	±	8.12	

While the HDL-c level in patients with EH was not signifinantly lower than that of the control group, the HDL-c lecel in the subgroup of EH with positive MA was significanlty lower when compared with that of EH with negative MA. There was also found a significant difference on the same parameter between EH with positive MA and controls.

Comparing the LDL-c values, we found similar changes, bu in the inverse sense. Table 7.

Table 7 - Changes of LDL-C on the same groups

	LDL - C				P
	Cases	$\bar{x}$	±	σ	
Gr. of control	16	93.73	±	27.08	n.s. p < 0.05
HTA	24	112.0	±	46.8	
HTA (microalb +)	13	128.76	±	56.02	p < 0.05
HTA (microalb -)	11	92.18	±	21.8	

Patients with EH in general had higher levels of LDL-c in comparison with the control group, but the difference was not significant. On the other side, it was found a significanlty higher mean level of LDL-c in patients with EH and positive MA when compared to patients with EH and negative MA. The difference between patients with EH and positive MA and the control group was also significant.

Discussion

Urinary excretion of albumin, especially of MA, is nowadays considered as an important marker of organ damage in both diabetic and non-diabetic patients. This study suggests that the prevalence of MA is higher in patients with EH. Albumin is a negatively charged protein with molecular radius 36A.

Albumin is filtered in the glomerulus at some extent, but there is only 20 mg/d albumin excreted in the definitive urine and this suggests an efficient tubular reabsorption. Even during physical efforts in normal persons, the daily excretion of albumin does

not exceed the level of 20 mg (4). But in EH there is found a high prevalence of MA.

One study shows that 54% of patients with EH had positive MA. Other authors found it in 15-30% of patients with EH (4,5,6). In a recent study, Bianchi et al (7) found MA in 40% of patients with EH.

But what should be the reason of albumin excretion in EH? One cause of positive MA could be intrarenal hemodynamic changes in EH. It is observed than in nontreated patients with EH, there is a subgroup with high renin activity after captopril supplementation and these patients have high levels of albumin excretion and increased filtration fraction (8).

Beyond that, it is observed that patients with MA do not have specific histologic lesions of the glomerular basement membrane and of the interstitium (9). It is observed a lower negative charge of glomerular basement membrane in diabetic patients. This phenomenon is linked with the decreased content of heparansulphate - proteoglican in the basement membrane (10). This alteration contributes to the urinary excretion of albumins in diabetics (11).

Is it possible that decreased tubular reabsorption is the cause of MA?

Until now, there is no evidence of tubular defects in patients with EH. In particular, there is no evidence of increased excretion of proteins of tubular origin (12).

Secondly, alterations of HDL-c and LDL-c seric profile were found in patients with positive MA and these findings were significanlty different from those of the control group and also from patients with EH without MA. All these suggest the existance of an atherogenic risk factor in patients with EH and positive MA. Bianchi et al, also found an increased Lp(a) seric level in these patients (13,14). Others, in studies with much larger groups of patients confirm that MA is associated with increased LDL-c / HDL-c ratio, decreased HDL-c levels and even increased uric acid levels (1).

Lastly, during interesting experimental studies, it is observed that inhibition of mitric oxide sinthase causes albuminuria and it would be of value for the future to study if abnormal activity of nitric oxide sinthase can cause albuminuria.

According to our findings of a more frequent albuminuria in EH and reassuming the up-to-date studies, we can say that MA reflects BP level. It is further observed that BP lowering causes a decreased albumine excretion in patients with EH, indipendently from the antihypertensive drug used (12). The same thing is observed in patients with type 2 diabetes (15).

It is also reported that the age has also a certain influence on the level of MA, In our study the age was greater in patients with EH and MA (mean age 50 +/- 11.24) but the difference was not significant.

Our findings also suggest that abnormalities of lipoproteins with atherogenic potential in patients with positive MA can contribute to a greater cardiovascular morbidity and mortality.

Today, the link between albuminuria and cardiovascular risk factors is not well known. It is said that proteinuria reflects hypertensive lesions in renal microcirculation or that MA in general is a marker of endothelial barriers dysfunction (16).

Concluding, we can say that monitoring of albumin excretion in patients with EH is of great importance for studying the efficasy of antihypertensive therapy, the evaluation of the risk in renal dysfunction and assessing the cardiovascular risk.

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