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Original Research Article

Diagnostic value of homocysteine and albumin in dialysis patients

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Abstract

Circulating homocysteine is often elevated in chronic kidney disease and end-stage renal disease (ESRD) patients. Hyperhomocysteinemia is a risk factor for cardiovascular disease (CVD). Serum albumin is usually decreased in these patients.Methods: We measured serum homocysteine and albumin concentration on a biochemistry auto analyser Cobas Integra 400 at the clinical laboratory of University Hospital – Pleven. To determine serum albumin and homocysteine, we used the Roche assay test. Using ROC analysis we evaluated the sensitivity and specificity for each parameter - for homocysteine sensitivity - 62.5% and specificity - 55.8% for the albumin, the sensitivity is 69.2%, and specificity - 68.8%. The area under the ROC standard was defined too. (AUC) - coefficients for cardiovascular accident. Respectively AUC (homocysteine) is 0.632 and AUC (albumin) is 0.757. Using a statistical program we managed to compose the relation of cardiovascular disease by logistic regression. The results of our study show that serum albumin, and homocysteine may be considered as useful and important laboratory parameters for assessing the risk of vascular disease in patients on hemodialysis. Both indicators can be used as predictors of vascular risk in patients on dialysis.

Keywords: Albumin, Cardiovascular disease, Chronic Kidney Disease (CKD), Homocysteine

INTRODUCTION

Homocysteine (Hcy) is a sulfur-containing amino acid and it is a mediate product in the metabolism of methionine. Methionine is a powerful antioxidant that neutralizes free radicals in the body that are formed by the action of a number of toxic or inflammatory agents and it has anti-sclerosis effect. Many studies suggest that this amino acid has a favorable effect on the lipid metabolism and it lowers cholesterol. For this transformation in the body are needed folic acid and vitaminsB, vitamin B12 / cobalamin / vit. B6 / pyridoxine / vit.V2 and riboflavin . Violations in the balance of the formation and removal of homocysteine could lead to changes in its plasma concentrations.

In the overall population the slightly increased plasma levels of total homocysteine (tHcy) are associated with increased cardiovascular risk (Danesh and Lewington, 1998; Homocysteine Studies Collaboration, 2002; Wald et al., 2002). The normal range of tHcy is 3-15 umol / l but many factors can influence this level (Refsum et al., 2004). Except for nutritional vitamins deficiencies, genetic renal sparsity is one of the most common reasons for the clinical hyperhomocysteinemia. Patients with endstage of renal disease (ESRD) typically have 2-3 ways higher levels of tHcy.Pervasion of hyperhomocysteinemia in this exact patient group is over 90% (Suliman et al., 2002; Suliman et al., 2000; van Guldener et al., 1998). Although some processes may explain the correlation between renal function and higher plasma concentrations of tHcy, the exact mechanism is not yet fully clear.

Several studies have demonstrated the link between high levels of tHcy and the risk of vascular disease in the general population. Other studies have reported a link between high levels of tHcy in patients with chronic renal impairment and increased mortality or the risk of cardiovascular disease (Chauveau et al., 1993; Bachmann et al., 1995; Robinson et al., 1996; Jungers et

Table 1. Sensitivity and specificity of parameters

Parameter	cut-off	Sensitivity (%)	Specificity (%)
Alb	≤37,20	69,2	68,8
Hcys	≥ 47,30	62,5	55,8

Table 2. AUC - coefficients for vascular accident

Parameter	AUC	SE	p	95% CI	
Alb	0,757	0,070	0,001	0,620	0,893
Hcys	0,632	0,080	0,089	0,476	0,788

al., 1997; Manns et al., 1999; Kunz et al., 1999). Among the many suggested mechanisms that could explain the relation between hyperhomocysteinemia and cardiovascular disease in patients with end stage renal disease(ESRD), is the endothelial dysfunction (the most common in this group) which could be one of the most important ones. Actually, prolonged exposure of endothelial cells to the Hcy decreases the production of nitric oxide and endothelium-dependent vasodilation, (Kalantar-Zadeh et al., 2004). The concept of Hcy-mediated endothelial dysfunction was confirmed by a group of healthy adults with high levels of Hcy (Weiss et al., 2003). Research shows that the decline in cardiovascular events may be due to or be caused by varying degrees of reduction in the level of tHcy.It can alsodeflate the conceptthat the slight hyperhomocysteinemia is cardiovascular risk factor (Woo et al., 1997; Doshi et al., 2003). It is also considered the likelihood of the reduced form of Hcy, rather than tHcy to be the fraction which has toxic effects on blood vessels. In fact, Hoffer and Co. Yap et al. (2000) reported that the level of the reduced form of Hcy increases in parallel with tHcy level in both groups of patients –patients with renal failureand healthy individuals. Another interesting mechanism that can cause Hcy vascular damage was offered recently by Ingrosso and Co. (Hoffer et al., 2001). They consider that high levels of Hcy in dialysis patients induces toxicity by an increase in the overall hypomethylation DNA which is associated with a defect in the expression of genes regulated by methylation, and also that the additives of folic acid recovered DNA methylation, therefore by this way abnormal gene expression are being corrected. Among other factors that may affect the level of tHcy in patients undergoing hemodialysis are hypoalbuminemia, malnutrition and inflammation (interrelated factors that may initiate or worsen atherosclerosis). The efficient tHcy exists primarily as a form of protein-bound to albumin. Albumin is the main Hcy-binding protein, and this is reflected in the positive correlation between the levels of tHcy and serum albumin, as reported in dialysis patients (Suliman et al., 2000; Kalantar-Zadeh et al., 2004). In tracking patients on hemodialysis for 12 months during the dialysis treatment, we confirm the strong correlation between baseline tHcy and serum albumin, and the changes in tHcy levels and changes in serum albumin.

MATERIALANDMETHODS

In our study, we studied 120 hemodialysis patients, females and males aged from 18 to 80 years, in a V-stage CKD. All studied patients have consented to their results to be used for scientific purposes.

The biological material used for the determination of homocysteine and serum albumin was free of hemolysis and lipemia. All samples were analyzed by a biochemical analyzer Cobas Integra 400 in a Medical diagnostic laboratory of University Hospital "Dr. George Stransky" - Pleven. The used test for homocysteine is based on the principle of testing the enzymatic cycle and evaluates the product from the conversion of cosubstrate instead of testing itself cosubstrate or the products from the conversion of homocysteine. The concentration of homocysteine in the sample is proportional to the amount of NADH, NAD +. To determine the albumin we used the Roche assay test.The reference values which are accepted for both parameters for healthy individuals of the Bulgarian populationare:albumin35–55g/l, andHcy<12umol/l.

After the initial measurement of serum homocysteine and albumin, the patients were tracked during one year within six visits for development of cardiovascular event (heart attack or stroke) or death due to such. In 18 patients (10 women and 8 men) haveoccurred vascular events - heart attack or stroke, compared with 15 of them whose outcome ended up fatal.

RESULTS

In our studies we used ROC analysis that evaluated the sensitivity and specificity for each parameter - for homocysteine sensitivity is 62.5% and specificity - 55.8%, for the albumin, the sensitivity is 69.2%, and specificity - 68.8% (Table1) . The area under the ROC standard was

Table 3. Logistic modelrelationvascularaccident- Hcys

	B	S.E.	Wald	df	p	OR	95% CI	
Hcys			7,284	2	0,026			
Hcys (40-50)	0,710	0,697	1,036	1	0,309	2,034	0,518	7,979
Hcys (>50)	2,367	0,899	6,932	1	0,008	10,667	1,831	62,133
Constant	-2,590	0,599	18,724	1	<0,001	0,075		

Table 4. Logistic modelrelationvascularaccident- Alb

	B	S.E.	Wald	df	p	OR	95% CI	
Alb	-0,242	0,068	12,555	1	<0,001	0,785	0,687	0,898
Constant	6,976	2,441	8,166	1	0,004	1071,028		

Table 5. Logistic modelrelationvascularaccident– (Hcys, Alb)

	B	S.E.	Wald	df	p	OR	95% CI	
Alb (<35; >=35)	-2,625	0,673	15,189	1,000	<0,001	0,072	0,019	0,271
Hcys			7,775	2,000	0,020			
Hcys (40-50)	1,452	0,794	3,339	1,000	0,068	4,270	0,900	20,264
Hcys (>50)	2,987	1,077	7,696	1,000	0,006	19,834	2,403	163,695
Constant	-1,439	0,645	4,978	1,000	0,026	0,237		

defined too (AUC) - coefficients for cardiovascular accident.Respectively AUC (homocysteine) is 0.632 and AUC (albumin) is 0.757 (Table 2). Using a statistical program we managed to compose the relation of cardiovascular disease by logistic regression. We make Logistic model relation vascular accident –Hcys (Table 3), vascular accident – Alb (Table 4) and vascular accident – Hcys,Alb (Table 5).

DISCUSSION

Our researches showed that homocysteine and albumin were positively associated with vascular risk in patients on hemodialysis. We found that the sensitivity of homocysteine is slightly lower - 62.5 % compared with this albumin - 69.2%. However, when albumin specificity is significantly higher - 68.8%, than that of the homocysteine - 55.8%, .It means that low levels of albumin in the dialysis patients are more strongly associated with increased risk of heart attack or stroke. The area under the ROC standard and both parameters respectively AUC (Hcy) - 0.632 and AUC (albumin) - 0.757. This indicates that the diagnostic value of the albumin is significant (p <0.05) and exceeds 0.66. With diagnostic value is also the homocysteine (p = 0.089). Although the p exceeds the critical point of 0.05, yet less than 0.10.It indicates that homocysteine may also be used as a diagnostic test with respect to the risk of vascular events in patients on dialysis.

Regarding the logistics model of the relation risk of vascular intsident- Hcys it should be stated that the patients with values of homocysteine higer than 50 umol/l are approximately 11 times more but with less risk of cardiovascular disease (heart attack or stroke)of patients with Hcys less than 40 umol/l.

In the connection vascular accident - albumin shows that the model was statistically significant (p <0,01; 95% CI <1). If the patient increases albumin by 1 g/l, the risk of heart attack or stroke will be reduced with 21.5%.Ultimately, it is seen that the increased homocysteine can be regarded as a risk factor for vascular risk in dialysis patients, as well as low serum albumin, but besides the albumin is protective factor, because with the increase of its values the risk of infraction or stroke decreases.

CONCLUSIONS

The results of our study show that serum albumin, and homocysteine may be considered as useful and important laboratory parameters for assessing the risk of vascular disease in patients undergoing hemodialysis. Both indicators can be used as predictors of vascular risk in patients on dialysis.Very important in our study is that we proved that albumin is not only a predictable but also protective factor for the risk of vascular disease in patients on dialysis.

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