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Serum erythropoietin level in anemia of chronic kidney disease - experience of a Romanian medical centre

Nivelul eritropoietinei serice în anemia din boala renală cronică - experiența unui centru medical românesc

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Abstract

In this study, different aspects of anemia in chronic kidney disease have been observed, starting from the fact that the severity of anemia is associated with the degree of kidney dysfunction, the main cause being the erythropoietin deficiency, which is synthesized mostly by the kidneys. 58 persons were included in this study, 19 patients with non-dialysis-dependent chronic kidney disease, 18 patients with chronic kidney disease who received kidney transplantation and 21 apparently healthy persons. We evaluated the serum level of erythropoietin, serum creatinine, proteinuria, the glomerular filtration rate, the erythrocyte parameters and the correlations between them. The prevalence of anemia in patients with chronic kidney disease was of 51.35%. The hemoglobin concentration in patients with kidney transplantation (12.4 ± 2.7 g/dL) and in non-dialysis-dependent patients (11.7 ± 1.4 g/dL) is significantly different compared to the apparently healthy persons (14.6 ± 0.8 g/dL) ($p<0.05$). In the case of the non-dialysis-dependent patients who were not treated with erythropoiesis- stimulating agents we found positive associations between the glomerular filtration rate and the number of erythocytes (r = 0.71), hemoglobin (r = 0.65) and hematocrit (r = 0.73), as well as negative associations between creatinine and the number of erythrocytes (r = -0.72), hemoglobin (r = -0.86) and hematocrit (r = -0.88). In patients with kidney transplantation and anemia we observed positive correlations between erythropoietin and the number of erythrocytes (r = 0.69), between the glomerular filtration rate and the number of erythrocytes (r = 0.78) and erythropoietin (r = 0.97), as well as negative correlations between proteinuria and the number of erythrocytes (r= -0.89), hemoglobin (r= -0.72), hematocrit (r = -0.72), and erythropoietin (r = -0.67), and between creatinine and the number of erythrocytes (r = -0.75) and erythropoietin (r = -0.86).

***Keywords**: anemia, chronic kidney disease, erythropoietin*

Rezumat

În acest studiu au fost surprinse aspecte ale anemiei din afecţiunile renale cronice, pornind de la faptul că severitatea anemiei se asociază cu gradul disfuncţiei renale, principala cauză fiind deficienţa eritropoietinei, care este sintetizată în cea mai mare parte de rinichi. Au fost implicate în studiu 58 de persoane, 19 pacienţi cu boală

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renală cronică nedependentă de dializă, 18 pacienţi cu boală renală cronică care au beneficiat de transplant renal şi 21 de persoane aparent sănătoase. Au fost evaluate nivelul eritropoietinei serice, proteinuria, creatinina serică, rata de filtrare glomerulară, parametrii eritrocitari şi au fost studiate corelaţiile existente între acestea. Prevalenţa anemiei la pacienţii cu boală renală cronică a fost de 51.35%. Concentraţia hemoglobinei pacienţilor cu transplant renal (12.4 ± 2.7 g/dL) şi a celor nedependenţi de dializă (11.7 ± 1.4 g/dL) diferă semnificativ de cea a persoanelor aparent sănătoase (14.6 ± 0.8 g/dL) (p < 0.05). La pacienţii nedependenţi de dializă, netrataţi cu agenţi de stimulare a eritropoiezei, am găsit asocieri pozitive între rata de filtrare glomerulară şi numărul de eritrocite (r = 0.71), hemoglobină (r = 0.65) şi hematocrit (r = 0.73), precum şi asocieri negative ale creatininei cu numărul eritrocitelor (r = -0.72), hemoglobina (r = -0.86) şi hematocritul (r = -0.88). La pacienţii cu transplant renal şi anemie au fost evidenţiate corelaţii pozitive ale eritropoietinei cu numărul eritrocitelor (r = 0.69), ale ratei de filtrare glomerulară cu numărul eritrocitelor (r = 0.78) şi eritropoietina (r = 0.97), precum şi corelaţii negative ale proteinuriei cu numărul eritrocitelor (r = -0.89), hemoglobina (r = -0.72), hematocritul (r = -0.72), eritropoietina (r = -0.67), şi ale creatininei cu numărul eritrocitelor (r = -0.75) şi eritropoietina (r = -0.86).

***Cuvinte cheie**: anemia, boala renală cronică, eritropoietina*

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Introduction

One of the major medical issues of the last past years is represented by the chronic kidney disease (CKD), whose prevalence in the general population reaches the value of 11% and is increasing (1). CKD is defined as a persistent kidney disease and the reduction in kidney function, the glomerular filtration rate (GFR) < 60 ml/min/1.73 m2 for 3 or more months, irrespective of the etiology. The presence of the chronic kidney disease is established based on the level of the kidney function, according to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NFK-KDOQI) criteria of diagnosis and classification (2) (Table I).

Kidney diseases with progressive renal insufficiency are usually accompanied by moderate or severe hypoproliferative anemia (3). Anemia was defined, according to the World Health Organization (WHO) criteria, as a hemoglobin value (HGB) of < 13 g/dL for men, respectively < 12 g/dL for women (2). In patients with advanced stages of chronic kidney disease, the etiology of anemia is multifactorial – the decrease of erythrocyte production, the increase of the erythrocitary destruction because of the intravascular or extravascular hemolysis, as well as the increase of blood loss (4). There is a combination between the decrease in the lifespan of the circulating erythrocytes, secondary to uremia, and an insufficient response of the erythropoietin (EPO) production, because of the kidney disease. During the evolution of the kidney disease a progressive decrease of the glomerular filtration rate and of the hemoglobin concentration has been noticed. Anemia often appears in the chronic kidney disease at GFR under 30-35 mL/min/1.73 m2 (5), and is normocytic normochromic with a normal or low number of reticulocytes (6). The reduction of the erythropoietin synthe-

Table I. The stadialization of chronic kidney disease according to the Kidney Disease Outcomes Quality Initiative

Stage	Description	GFR (mL/min/1.73 m2)
I	Kidney damage with normal or high GFR	≥ 90
II	Kidney damage with slightly low GFR	60 - 89
III	Moderate low GFR	30 - 59
IV	Severe low GFR	15 - 29
V	Kidney decompensation (uremia)	< 15

sis is proportional to the degree of excretory impairment. The main problem is not constituted by the total loss of the EPO production, but by the lack of an adequate response to the degree of anemia (4). Anemia represents an important cause of morbidity and mortality in patients with reduced glomerular filtration rate (7). The use of the erythropoiesis-stimulating agents (ESA) has significantly contributed to the improvement of the anemia treatment and of the quality of life of the patients with chronic kidney disease (8). The aim of the study consists in establishing the correlations between the level of serum erythropoietin, anemia and the chronic kidney disease, in order to understand more clearly the manner how the deficiency of kidney function is accompanied by the reduction of the erythropoietin synthesis, followed by the decrease of bone marrow erythropoiesis, and reflected in the values of the reticulocytes, erythrocytes, hemoglobin and hematocrit.

Material and methods

The study was carried out between March 2011 and March 2012. The study protocol was approved by the Ethics Committee of University of Medicine and Pharmacy Tîrgu Mureş and the study was conducted in accordance with the Helsinki Declaration. 58 persons were included in the study: 37 patients with chronic kidney diseases – 19 non-dialysis-dependent, 18 with a kidney transplantation; 21 apparently healthy persons (H), with similar age. They were hospitalized or were under ambulatory surveillance in the Departament of Nephrology of the Clinical Hospital Mureş, in the Departament of Nefrology and in the Specialized Ambulatory Adults of the Emergency Clinical Hospital Tîrgu Mureş, after obtaining the written informed consent of each person included in this study. The patients with CKD were selected on the basis of the diagnosis established according to the present international criteria. The patients who have recently received transfusions of blood or blood components were excluded from this study.

1. Methods of clinical evaluation: data referring to the diagnosis of the chronic kidney disease, stages II-IV, according to the KDOQI (2), the presence of anemia and/or other associated diseases, and the treatment with erythropoiesis-stimulating agents.

2. Methods for evaluating the kidney function: the quantitative determination of the total proteins in the 24 hours urine through the ultrasensitive method with pyrogallol red and sodium molybdate (the Konelab 30 analyzer, Spinreact); the determination of the serum creatinine level through the kinetic alkaline picrate method (Architect c8000 analyzer, Abbott) and calculating the glomerular filtration rate, according to IDMS (Isotope-Dilution mass Spectrometry).

To estimate the GFR, the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula was used:

GFR = 141 x min(Scr/κ,1)α x max-(Scr/κ,1)-1.209 x 0.993Age x 1.018 [for women] x 1.159 [for the black race]

where Scr is the serum creatinine (mg/dL); $\kappa = 0.7$, for women, or 0.9, for men, α is -0.329, for women, or -0.411, for men; min indicates the minimum Scr/κ or 1, and max indicates the maximum Scr/κ or 1 (9).

3. Special methods: the determination of the erythropoietin serum level using the chemiluminescent immunometric method in the solid phase (Immulite analyzer, Siemens). The reference values were established on the basis of the literature data and of the manufacturer recommendations (3.7-29.5 mUI/mL).

4. Hematologic methods for the evaluation of anemia: the complete blood count by measuring, numbering and calculating the hematological parameters (Cell-Dyn 3700 analyzer, Ab-

bott); determining the reticulocyte number (RT) – supravital stain with „brilliant cresyl-blue" (10); calculating the reticulocyte production index (RPI) – according to KDOQI:

RPI = RI/the maturation time. The reticulocyte index (RI) is calculated by reporting the absolute number of reticulocytes of the patient to the absolute number of reticulocytes of a healthy person (11). RPI > 3 indicates hyper-regeneration, meaning the proliferative response of bone marrow is adequate to the degree of anemia. RPI < 2 indicates hypo-regeneration indicating an inadequate bone marrow response to the degree of anemia (12).

The determinations were carried out in the Medical Analysis Laboratory of the Emergency Clinical Hospital Tîrgu Mureş.

5. Statistical methods: the statistical analysis was performed using Microsoft Excel 2003 and GraphPad InStat version 3.0. Means were compared using Student's t-test. The Pearson correlations coefficient was calculated. The results are considered significant in case of $p < 0.05$.

Results

The patients involved in the study were evaluated considering characteristics referring to age, sex, the stage of the disease, the basic kidney disease, comorbidities and treatment. The mean age of the apparently healthy persons was of 55 ± 17 years, and that of the patients with CKD was of 53 ± 15: the non-dialysis-dependent patients had the mean age value of 58 ± 17 years and those with a kidney transplantation the mean age value of 47 ± 11 years. The mean age of transplantation was of 41 ± 13 years. From the patients with CKD, 20 (54.05%) were men and 17 (45.95%) were women, and from the group of the apparently healthy persons, 11 (52.38%) were men and 10 (47.62%) were women. The kidney disorders were represented as follows: chronic glomerulonephritis (48.65%), polycystic kidney disease (15.79%) and chronic tubulointerstitial nephropathy (13.51%). The most frequent diseases associated with CKD are: arterial hypertension (70.27%), anemia (51.35%), secondary hyperparathyroidism (24.32%), ischaemic heart disease (21.62%) and diabetes mellitus (18.92%).

The patients with chronic kidney diseases were constituted into 2 groups: 19 (51.35%) patients with non-dialysis-dependent chronic kidney disease (CKD-ND), stages II-V (Table I), 9 (47.37%) men and 10 (52.63%) women, 6 (31.58%) without anemia and 13 (68.42%) with anemia, 8 (61.54%) patients being treated with ESA; 18 (48.65%) patients with post transplantation chronic kidney disease (CKD-T), stage V, 11 (61.11%) men and 7 (38.89%) women, 12 (66.67) without anemia and 6 (33.33%) with anemia, one patient being treated with ESA.

The values of the erythrocyte parameters, the serum level of erythropoietin and the indicators of the kidney function – proteinuria, serum creatinine, GFR were analyzed (Table II).

The patients from the CKD-ND group were distributed into 2 subgroups according to the presence or absence of the ESA therapy. The mean values of HGB and EPO in the subgroup that was not treated with ESA were of 12.1 ± 1.5 g/dL, respectively 16.9 ± 9.2 mUI/mL, and in the subgroup treated with ESA were of 11.0 g/dL ± 1.0 g/dL, respectively 31.5 ± 18.3 mUI/mL.

The patients with CKD-T were separated into 2 subgroups according to the presence or absence of anemia. The mean values of HGB and EPO in the subgroup without anemia were of 14.0 ± 1.2 g/dL, respectively 15.3 ± 5.8 mUI/mL, and in the subgroup with anemia not treated with ESA were of 9.7 ± 1.7 g/dL, respectively 20.6 ± 19.8 mUI/mL.

The associations between the level of serum erythropoietin level, erythrocyte parameters and indicators of the kidney function were evalu-

Table II. Intergroup comparisons of the average values of the erythrocyte parameters, serum erythropoietin and the indicators of the kidney function

	CKD-ND		CKD-T		H	
	mean/ median	±SD/ min-max	mean/ median	±SD/ min-max	mean/ median	±SD/ min-max
RT %	2.1	0.9	2.3	0.7	1.1	0.2
RPI	1.27	0.55	1.79	0.81	1.18	0.24
RBCx106/µL	3.92	0.53	4.28	0.98	4.86	0.24
HGB g/dL	11.7	1.4	12.4	2.7	14.6	0.8
HTC %	35.8	4.2	38.3	8.3	44.2	2
HEM pg/E	29.8	1.5	29.1	1.6	30.1	0.9
CHEM g/dL	32.6	0.5	32.4	0.4	33.1	0.6
VEM fL	91.6	4.7	89.7	4.8	90.9	2.5
EPO mUI/mL	19.4	6.0 - 64.9	14.5	5.6 - 63.8	14.6	6.1
Proteinuria g/24h	0.502	0.146 - 2.605	0.261	0.029-3.832	-	-
Creatinine mg/dL	2.23	0.77 - 8.80	1.15	0.75 - 4.52	0.76	0.66 - 0.98
GFR mL/min/1.73m2	31	7-82	70	13 - 101	94	62 – 125

ated (Table III, IV). In patients with CKD who received ESA treatment there are no significant correlations between the serum level of erythropoietin, erythrocyte parameters and indicators of the kidney function (Table III).

Significant correlation were represented graphically (Figure 1, 2).

Discussions

The mean age of the patients with CKD-T in our group was 47 years, similar to that reported by a study carried out in Germany - 48 years (13), and the mean age of transplantation was 41 years, close to that announced by TRESAM (The Transplant European Survey on Anemia Management) - 45 years (14). In the patients

Table III. Associations between the level of serum erythropoietin, erythrocyte parameters and the indicators of the kidney function in patients with chronic kidney disease not treated with erythropoiesis-stimulating agents and in the apparently healthy persons

	CKD-ND				CKD-T				H		
	repo	rpro	rcrea	rgfr	repo	rpro	rcrea	rgfr	repo	rcrea	rgfr
RT	0.48	-0.67	-0.48	0.07	-0.24	0.28	0.52	-0.60	0.44	0.37	0.02
RPI	0.19	-0.62	-0.50	0.28	-0.27	0.22	-0.30	0.25	0.38	0.35	0.00
RBC	-0.10	0.44	-0.72	0.71	-0.07	-0.05	-0.70	0.66	0.25	0.19	0.51
HGB	0.14	0.62	-0.86	0.65	-0.16	-0.17	-0.67	0.66	0.22	0.47	0.45
HTC	0.16	0.50	-0.88	0.73	-0.18	-0.13	-0.66	0.65	0.18	0.35	0.39
EPO	-	0.20	-0.28	-0.17	-	-0.26	-0.36	0.40	-	0.32	-0.06
Creatinine	-	0.05	-	-	-	0.55	-	-	-	-	-
GFR	-	-0.18	-0.68	-	-	-0.59	-0.94	-	-	-0.10	-

Table IV. Associations between the level of serum erythropoietin, erythrocyte parameters and the indicators of the kidney function in patients with chronic kidney disease without/with anemia not treated with erythropoiesis-stimulating agents

	CKD-T without anemia				CKD-T with anemia			
	repo	rpro	rcrea	rgfr	repo	rpro	rcrea	rgfr
RT	0.11	0.32	0.22	-0.29	-0.72	0.10	0.39	-0.61
RPI	-0.20	0.48	0.50	-0.36	-0.31	-0.49	0.02	-0.16
RBC	-0.54	0.43	0.57	-0.31	0.69	-0.89	-0.75	0.78
HGB	-0.59	0.03	0.23	0.05	0.42	-0.72	-0.50	0.52
HTC	-0.59	0.11	0.28	0.00	0.35	-0.72	-0.48	0.47
EPO	-	-0.34	-0.49	0.42	-	-0.67	-0.86	0.97
Creatinine	-	0.93	-	-	-	0.78	-	-
GFR	-	-0.78	-0.85	-	-	-0.76	-0.95	-

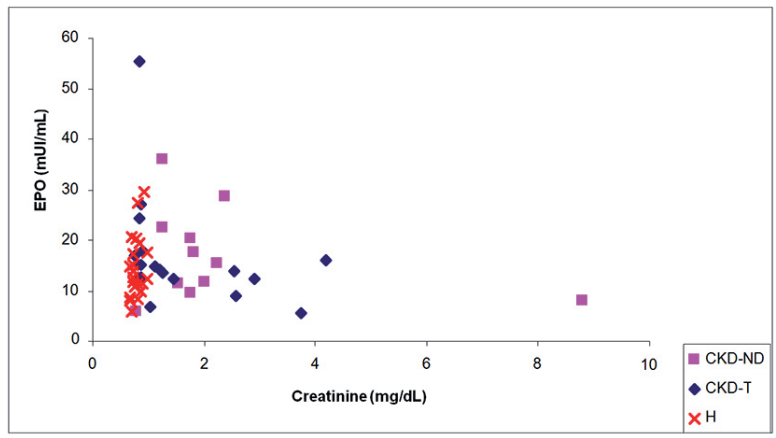

Figure 1. The graphic representation of the distribution of the patients not treated with ESA from the CKD-ND, CKD-T and apparently healthy persons groups considering level of the erythropoietin and creatinine.

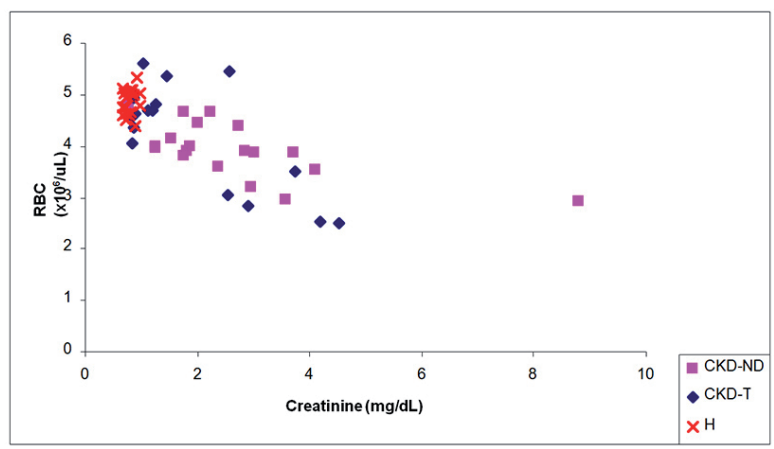

Figure 2. The graphic representation of the relation between creatinine and RBC in patients with CKD-ND (r = -0.72) and CKD-T (r = -0.70), compared to the apparently healthy persons (r = 0.19).

group the sex distribution men:women is 1.18:1, similar to the sex distribution in the control group, 1.10:1.

The increased value of creatinine indicates kidney dysfunction (15). Both creatinine and GFR, in patients with CKD-ND and patients with CKD-T, reflect the degree of the renal deficiency (Table II). The persistent proteinuria is considered to be the main marker of the kidney damage (16), its values being, both in the CKD-ND group and in the CKD-T group, over the physiological limits (Table II).

Anemia is often present in patients with CKD, more than half (51.35%) of the patients included in our study having anemia. CDC (Centers for Disease Control) reports showed that among the non-dialysis-dependent patients 68.00% had anemia (17), and this is similar with our results, 68.42% of our patients with CKD-ND having anemia. A great prevalence of anemia was observed, in a multicentric study, in patients with different stages of CKD, indicating that for a level of HGB under 12 g/dL, the evaluation of anemia etiology should be initiated (18). For patients with a HGB level under 11 g/dL, introduction of the ESA therapy is recommended (18, 19). In our study the CKD patients in stage II did not present anemia, the patients in stage III had a prevalence of anemia of 44.44%, and in the stages IV and V, all the patients with CKD-ND had anemia, 61.54% of the patients with CKD-ND being treated with ESA. A significant number of patients who have benefited of a kidney transplantation had persistent anemia (20). The renal dysfunction is the most important factor of risk for post transplantation anemia (PTA). Anemia can be aggravated by the immunosuppressive medication, especially by the cyclosporine, mycophenolate mofetile and azathioprine (21). The prevalence of PTA in our study is 33.33%, close to the value reported by the European Transplant Survey - 38.60% (22). In our study, men had a slightly higher prevalence of anemia compared to women (55% to 47%). There is a higher prevalence of anemia associated with CKD in older patients (23). In our study the prevalence was 66.67% in patients over 60 years, probably as a consequence of the lower glomerular filtration rate, of the increased risk of developing uremia and of the complex pathology specific to the age. A higher erythrocyte regeneration rate was highlighted in the group with kidney transplantation, as RPI (1.79 ± 0.81) differs significantly from the value in the apparently healthy group (1.18 ± 0.24) ($p < 0.05$), because the transplanted kidney synthesizes endogenous erythropoietin, with a stimulating effect on the bone marrow erythropoiesis. The RPI in the CKD-ND group (1.27 ± 0.55) is close to that in the apparently healthy group. Anemia associated to CKD is hypoproliferative, the reticulocyte values and RPI < 2 indicating an inadequate bone marrow response to the degree of anemia. The erythrocyte number, the hemoglobin and the hematocrit in the CKD-T group were higher, but not significantly, than those in the CKD-ND group (Table II). The hemoglobin concentration in the CKD-T and CKD-ND groups are lower compared to that in the apparently healthy group ($p < 0.05$). The values of the erythrocyte indices does not differ significantly in the groups with CKD from the apparently healthy group because in most cases anemia is normochromic and normocytic.

The main cause of the anemia associated to CKD is erythropoietin deficiency (24). It was noticed that although the serum concentration of EPO was significantly higher in patients with CKD-ND who received ESA (31.5 ± 18.3 mUI/mL), compared with those who did not receive it (16.9 ± 9.2 mUI/mL) ($p < 0.05$), the HGB concentration was lower (11.0 ± 1.0 g/dL versus 12.1 ± 1.5 g/dL). This situation occurs probable because patients who need the ESA therapy are in advanced stages of CKD (mostly in IV and V stages) but also because of the inferior efficacy of the recombined EPO compared to the natural

EPO. Although the EPO level in patients with CKD-T and anemia not treated with ESA (20.6 ± 19.8 mUI/mL) is higher than in patients without anemia (15.3 ± 5.8 mUI/mL), that increase is not significant and also not adequate to the degree of anemia, a fact reflected by the mean HGB in patients with anemia (9.7 ± 1.7 g/dL), which is significantly lower compared with that in patients without anemia (14.0 ± 1.2 g/dL) ($p < 0.05$). The ESA treatment is necessary in the patients with CKD associated with anemia, and it has beneficial effects but also adverse effects, especially cardiovascular events (25), which are increasing with the concentration of serum erythropoietin. Thus, it is important to establish the minimum doses sufficient to maintain the hemoglobin within values between 11-12 g/dL (19). Because of the individual biodisponibility variation, the ESA therapy must be conceived and applied in a particularized way, taking into consideration comorbidities, age and physical activity (26, 27).

The correlation coefficients had low values in the group of the apparently healthy persons and in that of the patients with CKD without anemia compared with the patients who had CKD associated with anemia. Strong positive correlations were found in the group of patients with CKD-ND not treated with ESA, between GFR and RBC, and between HGB and HTC (Table III). A strong negative association of creatinine with RBC and a very strong negative association with HGB and HTC was highlighted. A study that was carried out by researchers from Turkey observed the fact that the value of HGB was positively correlated to the creatinine clearance and negatively correlated to the level of the serum creatinine (15). The present study confirms these conclusions, as strong negative correlations of creatinine with RBC, HGB and HTC, as well as strong positive correlations between GFR and RBC, HGB and HTC were highlighted. In patients with CKD-T and anemia a series of associations were highlighted: EPO is strongly positively correlated with RBC; proteinuria is strongly negatively correlated with RBC, strongly negatively correlated with HGB, HTC, EPO and GFR, as well as strongly positively correlated with creatinine; creatinine correlates strongly negatively with RBC, GFR and EPO; GFR correlates strongly positively with RBC and with EPO (Table IV). The moderate and low associations in patients without anemia are the consequence of the negative feedback mechanism - the tissular oxygenation is sufficient, the concentration of HGB in the blood is normal, which inhibits the EPO synthesis. The significant associations in patients with anemia associated to CKD are due to the positive feedback mechanism – the tissular oxygenation is insufficient because the concentration of HGB is low, which stimulates the erythropoietin synthesis, but this is inadequate for the degree of anemia.

The gradual decrease of the erythropoietin synthesis during the evolution of the chronic kidney disease can be remarked (Figure 1). The decrease of the erythrocyte number correlated with the increase of the creatinine is obvious (Figure 2). The images reflect the distribution of the apparently healthy persons as a well-delimited compact group, with the best kidney function, with the values of the erythrocyte parameters and the serum values of the erythropoietin in the reference interval. The group of the patients who received kidney transplantation partly interferes with that of the healthy persons and partly with that of the patients with CKD-ND. The explanation for this distribution consists in the fact that the patients with CKD-T presented a wide variation: in the case of the persons with normal function of the transplanted kidney, anemia can be corrected due to the endogenous erythropoietin synthesis, while to some persons it is possible to occur post transplantation anemia, with its characteristic aspects related to the functional state of the kidney graft and the immunosuppressive

therapy (28). The group of the non-dialysis-dependent patients has a distribution determined by the successive stages of the chronic kidney disease associated with anemia, prevalent in the advanced ones.

These associations constitute the support to demonstrate the relationship between the deficient kidney function and anemia, erythropoietin being the connection element, in the sense that the kidneys with structural and functional alterations synthesize insufficient erythropoietin to correct anemia. Anemia associated with CKD requires a treatment according to its complexity, in order to eliminate the deficiency of erythropoietin through the ESA therapy, as well as the insurance of the iron, vitamins and minerals intake, necessary for an efficient erythropoiesis.

Further studies with a larger number of patients are necessary in order to find out new and efficient therapeutic alternatives with minimal side effects.

Conclusion

During the evolution of the chronic kidney disease erythropoietin synthesis decreases, its level being inadequate to the degree of anemia, a fact reflected by the reticulocyte production index, as well as by the low values of the erythrocyte count, hemoglobin concentration and hematocrit. Following transplantation, the kidney function and anemia have a generally favorable evolution, but the manifestation of post transplantation anemia is possible. The severity of anemia is associated with the gravity of the chronic kidney disease, a fact supported by the correlations existing between the level of the serum erythropoietin, the erythrocyte parameters and the indicators of the kidney function, correlations that are not strictly linear and are more obvious in the advanced stages of the chronic kidney disease.

Abbreviations

CKD = chronic kidney disease
CKD-ND = non-dialysis-dependent chronic kidney disease
CKD-T = post transplantation chronic kidney disease
EPO = erythropoietin
ESA = erythropoiesis-stimulating agents
PTA = post transplantation anemia
RPI = reticulocyte production index
KDOQI = Kidney Disease Outcomes Quality Initiative
r = correlation coefficient
GFR = glomerular filtration rate
H = apparently healthy

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