EVOLUTION OF ANEMIA IN CHRONIC KIDNEY DISEASE PATIENTS

EVOLUÇÃO DA ANEMIA EM PACIENTES COM DOENÇA RENAL CRÔNICA

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ABSTRACT

Variations in hematocrit and hemoglobin values are constantly checked in patients with chronic kidney disease (CKD) on dialysis in order to monitor the anemia. Anemia and iron deficiency are the most frequent and severe nutritional deficiencies, acting as a cause of morbidity in individuals carrying CKD. The work aimed to monitor the evolution of laboratory parameters of chronic renal patients on dialysis of a clinic in the state of Paraná, Brazil, for twelve months, correlating them with the drug therapy (iron injection and EPO). This is a cross-sectional investigation of quantitative character, whose data were collected from the results of laboratory tests of 108 adult patients. The data showed that at the beginning of the study 86.1% of patients were anemic; the number of patients with serum iron less than 50μg/mL increased 27%, and the number of patients with TSAT<20% increased 129%. The results emphasize the importance of careful evaluation of laboratory values by the health professionals, especially the nephrology clinical team, who deal with patients with CKD through the identification and correction of clinical and laboratory factors that alter the clinical picture of the patient.

Keywords: Chronic renal disease. Anemia. Dialysis.

RESUMO

As variações nos valores de hematócrito e hemoglobina são constantemente avaliadas em pacientes com doença renal crônica (DRC) em diálise para controlar a anemia. A anemia e deficiência de ferro são mais frequentes e graves deficiências nutricionais, atuando como causa de morbidade em indivíduos portadores de DRC. O trabalho teve como objetivo acompanhar a evolução dos parâmetros laboratoriais de pacientes renais crônicos em diálise de uma clínica no estado do Paraná por doze meses, correlacionando-os com a terapia medicamentosa (injeção de ferro e EPO). Trata-se de uma pesquisa transversal de caráter quantitativo, cujos dados foram coletados dos resultados dos testes laboratoriais de 108 pacientes adultos. Os dados mostraram que, no início do estudo, 86,1% dos pacientes eram anêmicos; o número de pacientes com ferro sérico inferior a 50μg/mL aumentou 27%, e o número de pacientes com TSAT<20% aumentou 129%. Os resultados ressaltam a importância de cuidadosa avaliação dos valores de laboratório

pelos profissionais de saúde, especialmente a equipa clínica da área de Nefrologia, que lidam com pacientes com DRC, através da identificação e correção de fatores clínicos e laboratoriais que alteram o quadro clínico do paciente.

Palavras-chave: Doença renal crônica. Anemia. Diálise.

INTRODUCTION

The prevalence of hemodialysis in Brazil has increased in recent years from 24.000 in 1994 to more than 54.500 patients in 2002 (ROMÃO-JÚNIOR, 2004), and in 2009 it was estimated an approximate number of 77.589 dialysis patients, and a gross mortality rate of 17.1 (SESSO et al., 2010). Currently it is estimated that there is 91.314 patients performing dialysis in Brazil, being 84.5% from SUS (*Sistema Único de Saúde*) and 15.1% from others agreements. These 66.9% have 19 to 64 year old and 35.1% have hypertension as underlying disease (SOCIEDADE BRASILEIRA DE NEFROLOGIA, 2011). However, a recent study indicates that about 2.9 million Brazilians can submit one third or less of the glomerular filtration rate of normal individuals (FERNANDES; BASTOS, 2010).

With the increase of renal function loss on clinical manifestations, anemia is the often complication observed whose prevalence and intensity relates to the stage of renal disease and deficiency of erythropoietin (EPO) (ESCHBACH; ADAMSON, 1985) (CORESH et al., 2001). Other situations may contribute to the advent of anemia, such as: iron deficiency, blood loss, the hyperparathyroidism and inflammation (BRITTENHAM, 1995).

Deficiency of iron (Fe) is a severe nutritional deficiency that has high morbidity in individuals carrying chronic kidney disease (CKD) (WHO, 2001). Therefore, the patient's level of iron with CKD requires constant evaluation. Supplementation with iron ensures an adequate response to EPO in patients with CKD, since the iron bone marrow erythroid hypoplasia demands often exceeded amount of iron available for erythropoiesis (measured by percentage of transferrin saturation – TSAT) as well as stocks of iron (measured by serum ferritin). In most hemodialysis patients intravenous application of iron is necessary to achieve adequate stocks of iron (K/DOQI, 2006).

Most patients with CKD have anemia, normocytic and normochromic (ESCHBACH; ADAMSON, 1985). Anemia is associated with several physiological disorders in CKD, including decrease of oxygen use and release into the body (HORINA et al., 1993; MAYER et al., 1988; TEEHAN et al., 1989; ROBERTSON et al., 1990; BRAUMANN et al., 1991), increased cardiac output, cardiac area increased, ventricular hypertrophy, angina, congestive heart failure (HARNETT et al., 1995) (WIZEMANN; SCHAFER; KRAMER, 1993), reduction of mental acuity and cognition (WOLCOTT et al., 1989), alteration of menstrual cycles (RAMIREZ et al., 1994) and impairment of immune response (GAFTER et al., 1994). In addition, anemia can retard growth of pediatric patients (SCIGALLA et al., 1989). These abnormalities reduce the quality of life (EVANS; RADER; MANNINEN, 1990) and opportunities for rehabilitation in patients that survived CKD (LOWRIE et al., 1994). Monitoring the evolution of patients enables creating a therapy according to the physiological necessity of the organism, since clinical-laboratory parameters can change significantly over time.

Chronic renal disease is currently a public health problem worldwide, and that has been an increase in its incidence mainly due to the greater life expectancy, and an increase in the prevalence of diabetes mellitus and hypertension in population. The health expenditures in dialysis and renal transplant in Brazil exceed 1.8 billion a year (ROMÃO-JÚNIOR, 2004). The research for new therapeutic strategies is a constant attempt to improve the quality of life of patients. Thus, the aim of this paper is to describe and assess the evolution of chronic renal patients on hemodialysis with regard to the development of anemia, their treatment during the period of one year and correlate it with laboratory parameters.

Materials and methods

This is a cross-sectional study of quantitative character, whose data were collected through the records of the results of laboratory tests and monthly prescriptions of EPO and iron of 108 adult dialysis

patients from the city of Guarapuava, in the state of Paraná, Brazil. The following criteria were used to include patients in this study: 1) patient must have CKD; 2) be in dialysis for more than six months; 3) not have suffered kidney transplant in the past; 4) be over 18 years.

All adopted procedures to provide information have been assessed and approved by the Ethics Committee of Midwest State University – UNICENTRO, through the opinion letter 121/2009.

The laboratory data presented in this study were collected from January to December 2010. All laboratory examinations for this period were carried out by a laboratory located in Santa Tereza Hospital, in the city of Guarapuava.

The patients received exogenous EPO and 100mg of iron hydroxide saccharate (Fe III), up to 4 times a week. The doctors of the hemodialysis clinic adjusted the doses of EPO and Fe according to the patient's anemia and to prevent iron overload.

Data from the hematocrit (Ht) and hemoglobin (Hb) were obtained every 30 days, and dosages of serum iron and transferrin were obtained every 90 days. The index of transferrin saturation (TSAT) was also obtained through determination of iron and iron-binding.

The data were stored in a database and, at the end of the collection, the data were analyzed through descriptive statistics. The laboratory findings were presented through average ± standard deviation and

times a week, in the period of the study. The EPO was administered to all patients in the study. The EPO and iron administration was performed to patients whose results of the laboratory parameters of every 30 days of hematocrit and hemoglobin reached adjacent values to dialysis patients with CKD. The EPO administration was suspended as medical criteria through the analysis of hemoglobin and hematocrit.

A total of 60 men (89.5% of men) and 33 women (80.4% of women) presented anemia (Table 1), according to the criteria of *Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease* (K/DOQI, 2006) which considers anemic individuals those with Ht less than 33% for woman and less than 37% for man.

Table 1 – Percentage of anemic and non-anemic in relation to patient hematocrit values. Data obtained between January and December 2010 – Guarapuava, Paraná, Brazil

Parameter	Patients	
	Anemic	Non-anemic
Hematocrit	86.1% (n=93)	13.9% (n=15)

Source: Pachtman et al. 2010.

The average hematocrit of all patients at the end of six months and at the end of one year was 31±4.5 and 31±5, respectively. The data of laboratory parameters of Ht and Hb of patients are listed in Table 2.

Table 2 – Laboratory parameters of hematocrit (Ht) and hemoglobin (Hb) concentration of 108 patients in 2010. Data obtained between January and December 2010 – Guarapuava, Paraná, Brazil

Variable	Patients		
	Average (± SD*) (January – June)	Average (± SD) (July – December)	P value*
Hematocrit (Ht) (%)	31 ± 4.5	31 ± 5	> 0.05
Hemoglobin (Hb) (g/dL)	10.3 ± 1.3	10.4 ± 1.4	> 0.05

*SD: Standard deviation.
Source: Pachtman et al. 2010.

percentage using Graph Pad Prism® 5.01 (2001) and Microsoft Excel® 2007. Statistical significance was established by ANOVA in 5% (p<0.05).

Results and discussion
Prevalence of anemia

The sampling was composed of 108 patients, being 67 men (62%) and 41 women (38%). A total of 49 patients (45.4%) received 100mg of iron, 2 to 4

The iron administration during the period of the study gradually decreased, as demonstrated in Table 3. The iron administration aims to maintain adequate levels in a way that patients with CKD can achieve and maintain a Ht level of 33 to 37% (Hb 11 to 12g/dL) along with treatment with EPO.
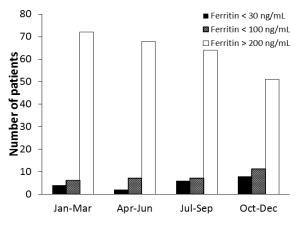
Table 3 – Number of patients receiving intravenous iron administration and percentage of patient receiving iron for each 3 months. Data obtained between January and December 2010 – Guarapuava, Paraná, Brazil

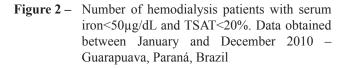|	Number of patients	
	# of patients receiving iron	% of patients receiving iron
Jan-Mar	48	44.4
Apr-Jun	35	32.4
Jul-Sep	36	33.3
Oct-Dec	35	32.4
Average	38.5	35.6

Source: Pachtman et al. 2010.

Figure 1 shows a decrease in the number of patients with ferritin>200ng/mL and an increase in the number of patients with ferritin<30ng/mL.
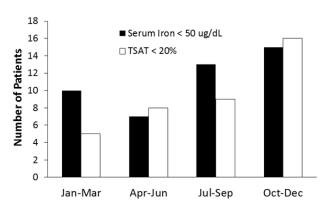
Figure 1 – Number of hemodialysis patients with ferritin values less than 30ng/mL, less than 100ng/mL and greater than 200ng/mL per quarter in 2010. Data obtained between January and December 2010 – Guarapuava, Paraná, Brazil

Source: Pachtman et al. 2010.

Figure 2 shows that during the year evaluated the number of patients with serum iron less than 50μg/mL increased 27%, and the number of patients with TSAT<20% increased 129%.

Figure 2 – Number of hemodialysis patients with serum iron<50μg/dL and TSAT<20%. Data obtained between January and December 2010 – Guarapuava, Paraná, Brazil

Source: Pachtman et al. 2010.

Table 4 shows the number of individuals with absolute and relative deficiency of iron according to the following criteria: ferritin<100μg/L and TSAT<20% for absolute iron deficiency, and ferritin<300μg/L and TSAT<30% for relative iron deficiency.

Table 4 – Patients with absolute and relative deficiency of ferritin. Data obtained between January to December 2010 – Guarapuava, Paraná, Brazil

	Absolute deficiency		Relative deficiency	
	Ferritin<100mg/L	TSAT<20%	Ferritin<300mg/L	TSAT<30%
Jan-Mar	4	6	8	14
Apr-Jun	9	5	21	13
Jul-Sep	14	9	35	10
Oct-Dec	19	16	42	24

Source: Pachtman et al. 2010.

In the study, an increase of individuals with ferritin and TSAT deficiency was observed in each quarter. The deficiency is considered relative or functional when the patient presents ferritin values between 100 and 300µgL and transferrin saturation between 20% and 30%. The administration of intravenous iron induces an improvement in hemoglobin level.

Conclusion

Changes in hematologic and biochemical variables of 108 patients were followed for a period of one year, and although the average values of hematocrit and hemoglobin of the patients remained similar in the first and second halves of the study, it was observed that the absolute and relative deficiency of iron increased, reflecting directly on the values of ferritin and TSAT. The intravenous administration of iron in quantities exceeding required for physiological phenomena promotes excessive production of cellular stress, but also progressively improves the ferric profile.

Evaluation of iron levels of the patients was carried out using ferritin and TSAT. The evolution of hematological parameters of patients observed in this study is similar to those described in the literature about nephrogenic anemia correction with intravenous iron therapy (TARNG; CHEN; HUANG, 1995; NATIONAL KIDNEY FOUNDATION, 1997; LUDAT et al., 2000; LIM et al., 1999; MIMIC-OKA et al., 2005). However, iron supplementation should be evaluated with caution due to possible side effects, particularly in high doses of intravenous iron (LIM et al., 1999; ROOYAKKERS et al., 2002; CAVDAR et al., 2003; MIMIC-OKA et al., 2005).

The worsening of CKD depends on interactions that involve several clinical factors, among others. Age, gender, diabetes, hypertension, proteinuria, anemia, obesity, metabolic complications, smoking and dyslipidemia are among the clinical factors, which together with genetic and environmental factors can aggravate the framework of CKD (BASTOS; KIRSZTAJN, 2011). Anemia is common in patients with CKD, and patients with lower values of hemoglobin have worse outcomes than those with higher values. Hemoglobin value <13g/dL for adult men and <12.0g/dL for women and men >65 years are

the criteria of Brazilian guidelines for the assessment of these patients (RIBEIRO-ALVES; GORDAN, 2007). The reserves of iron evaluated in the study by ferritin were considered appropriate when over 100µg/L and transferrin saturation greater than 20% in evaluated patients (BASTOS; KIRSZTAJN, 2011). However, absolute iron deficiency was explained in Table 4, where the number of patients with ferritin<100µg/L and TSAT<20% went from 4 to 19 and 6 to 16, respectively, over the year of the survey.

The fact that some patients do not reach adequate levels of iron, ferritin and TSAT (Table 3), even with a high dose of EPO, can be due to infectious complications or bleeds. The criterion used by clinical staff, in these cases, is to keep the dose of EPO and re-evaluate the patient after the acute phase of complication.

Treatment with EPO increases the rate of erythropoiesis, and therefore the demand for iron, which results in difficulty to maintain optimal levels of iron in hemodialysis patients when coupled with the substantial blood loss. The use of intravenous iron treatment is more effective against anemia associated with CKD in hemodialysis patients. However, hypersensitivity reactions may occur in this type of treatment, which would not occur in the treatment with oral iron (ESCÓRCIO et al., 2010).

The findings obtained in this study emphasize the importance of a careful evaluation of laboratory values on the part of health professionals, especially nephrologists who often deal with patients with CKD. The potential benefits of careful and judicious evaluation include identifying and correcting factors that worsen the clinical picture of the patient, for example, correction of laboratory values by obtaining the best biochemical parameters.

We declare no conflict of interest.

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