Editorial

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Anemia is an important complication in patients with chronic kidney disease (CKD). It generally starts when CKD has progressed to stage 3. At present, its diagnosis is generally made by the systematic determination of blood hemoglobin (Hb). It is more infrequently based on symptoms or clinical signs. Although the main causes of the anemia of CKD are a reduction in renal erythropoietin secretion but also deranged oxygen sensing by the kidney[1] numerous other causes may contribute as well. They need to be explored and treated, whenever possible. Iron deficiency is the most frequent one. It is easy to correct. Another frequent cause is the inflammatory state which is often assocaited with CKD. It is much more difficult to treat.

In the past 20 years several randomized controlled trials (RCTs) have been done to examine the question whether patients with CKD would benefit more from complete anemia correction by erythropoiesis stimulating agents (ESAs) than from only partial anemia correction. The result of the first large-scale RCT in chronic hemodialysis patients came as a surprise.[2] It showed against expectations that complete anemia correction led to a higher number of myocardial infarcts and deaths than partial correction. However, since all study patients suffered from congestive heart failure or ischemic heart disease nephrologists reasoned that the deleterious effects of raising Hb values to the normal range were probably limited to the particular subgroup of dialysis patients with severe heart disease. Therefore, several RCTs were then conducted in patients with CKD stages 3-5 before having reached the stage of renal replacement therapy. Unexpectedly, these trials again showed that complete anemia correction with ESAs did not lead to superior patient outcomes.[3-5] They actually pointed to the possibility of a higher risk of arterial hypertension, cardiovascular and cerebrovascular disease and mortality, thrombosis of the vascular access in those who required dialysis, and the occurrence or aggravation of cancer.

Moreover, several recent studies have shown that the contribution of iron deficiency to the anemia of CKD had been largely underestimated in the past, and that the I.V. administration of iron frequently led to an increase in Hb values. However, in contrast to the studies done with ESAs no RCT has ever been conducted with I.V. iron in patients with CKD. Thus we do not know for sure whether in the long run, I.V. iron is beneficial or harmful, especially when given in high doses and with high frequency. In addition, it remains uncertain whether the tolerance and adverse effects of the different presenty available I.V. iron brands are comparable or vary from one preparation to the other.

Because of the RCTs recently conducted with ESAs in patients with CKD the international institution KDIGO (Kidney Disease: Improving Global Outcomes) decided to set up new recommendations of best clinical practice, based on a rigorous evaluation by a group of international experts of the level of available evidence in the medical literature, with the assistance of a professional team in Boston, MA, USA. The goal was to update previous US recommendations by KDOQI reported in 2006 and partially revised in 2007, with particular attention being paid to the 6 RCTs published since 1998 et their conclusions with respect to morbidity and mortality. The KDIGO anemia guideline was published in a supplement of Kidney International in August 2012.[6]

The international character of the guideline mission adopted by KDIGO has been aimed at recommendations which should be applicable worldwide. However, the KDIGO language

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is English. Therefore translation into national languages is required. Moreover, health care systems and available resources are highly variable from one country to the other, so local and/or regional adaptations are generally required. Finally, the interpretation of available evidence by local authorities is not necessarily identical to that of the international expert group nominated by KDIGO.

For all these reasons, we would like to congratulate the nephrology community of Brazil to have set up Brasilian recommendations for the treatment of anemia in patients with CKD. They are not fundamentally different from the KDIGO guideline although there are some differences which deserve to be mentioned. The Brasilian recommendations for I.V. iron administration give more precise guidance as regards various Hb levels, allow serum ferritin to be raised up to 800 ng/mL, especially in those with functional iron deficiency, and more practical advice how to supplement iron. Concerning the correction of anemia by ESAs, the Brasilian recommendations allow for targets between 10 and 12 g/dL at any stage of CKD, not to be raised above 13 g/dL, and to individualize Hb targets based on considerations of possible harm (history of stroke and/or of cancer) and possible benefit (coronary artery disease, left ventricular hypertrophy), respectively.

The subsequent step will be to evaluate the adoption and practical application of these locally adapted recommandations to the CKD patient population throughout Brazil. We are confident that this will be done in the possible way and best interest of all those patients with CKD who suffer from anemia.

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