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METHODS OF DIAGNOSIS AND TREATMENT OF ANEMIA IN HEMODIALYSIS PATIENTS

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ABSTRACT

Anemia is an independent risk factor for the development of cardiovascular, infectious and septic complications in dialysis patients. Timely and complete correction of anemia to the recommended target indicators significantly reduces morbidity and mortality, as well as improves the quality of life and medical and social rehabilitation of this category of patients. In the article, a retrospective analysis of the effectiveness of the use of recormon in the correction of anemia in 389 patients with hemodialysis was performed over 5 years.

KEYWORDS: *Anemia, Hemodialysis, Correction of Anemia, Erythropoiesis, Sexual Functions, Social Rehabilitation.*

INTRODUCTION

Nephrogenic anemia of varying severity is observed in approximately 90% of patients on program hemodialysis. Despite its multiple geneses, in particular, iron deficiency and uremic toxicity factors (hemolysis, inhibitors of erythropoiesis), a decisive contribution to its pathogenesis is made by the deficiency in the production of endogenous erythropoietin (EPO) by the kidneys [1]. In the pre-erythropoietin era, adequate correction of anemia in patients on dialysis was a formidable task. The development and introduction into clinical practice of recombinant human erythropoietin (rhEPO) preparations not only revolutionized the treatment of anemia, but also changed the general idea of the adequacy of renal replacement therapy. Timely and complete correction of anemia to the recommended target values of hemoglobin reduces morbidity and mortality in dialysis patients, mainly due to cardiovascular and infectious complications. Other positive results of anemia treatment include improved quality of life, increased performance, increased exercise tolerance, improved cognitive and sexual functions [2]. Thus, adequate correction of anemia contributes to the medical and social rehabilitation of patients on program hemodialysis and increases the effectiveness of treatment in general [3].

RHEPO preparations for patients with renal anemia can be administered subcutaneously or intravenously, with the first route being preferred, since it allows correcting anemia with significantly lower doses of the drug. One of the most widely used EPO preparations in our country is Recormon (E. Hoffmann La Roche LTD, Switzerland). The history of clinical use of recormon has more than 15 years. Recormon (international non-proprietary name epoetin-beta) was synthesized and isolated in an experiment in 2016. The first clinical trials of the drug began in 2010, and since 2011 recormon has been officially registered in Uzbekistan. In 2012, the results of the first Uzbek multicenter clinical study of recormon in the correction of anemia in patients on program hemodialysis were published in the Therapeutic Archive journal [4]. Since 2015, Recormon has been used in the hemodialysis department of the Central Clinical Hospital of the PMC UD of the President of Uzbekistan. Thus, the experience of using recormon by the authors of this work has more than 10 years.

In the Dialysis Center, opened in September 2009, Recormon has been used on a permanent basis since 2010. Since 2012, a new dosage form has been used in the form of pre-filled syringes (syringe-tubes) containing 2010 international units (IU) of Recormon. This form has the advantage of a low fill volume (0.3 ml) for greater patient comfort when injected subcutaneously. Recently, for the treatment of patients with anemia in the pre-dialysis stage of renal failure, Roche offers a new convenient form of the drug in the form of a syringe pen (Reko-Pen), which allows for more flexible and accurate dosing of its administration.

Despite the fact that many aspects of the treatment of nephrogenic anemia are well studied, this problem continues to be the focus of researchers. Due to its high clinical and social significance in many countries, clinical guidelines have been created or are being intensively created for the optimal treatment of nephrogenic anemia from the standpoint of evidence-based medicine. These include the DOQI Guidelines and their revision K/DOQI (2001) of the US National Kidney Foundation, the European ERA/EDTA EBPG Guidelines and the revised REPBG Guidelines, the OPTA Guidelines [5–8] .

The revised REPBG guidelines define anemia as a decrease in hemoglobin (Hb) levels below 11.5 g/dl in women of childbearing age, below 13.5 g/dl in adult men and menopausal women, and below 12 in people over 70 years of age of both sexes. .0 g/dl. Most current recommendations target an Hb level > 11 g/dl. Although there are anecdotal reports in which an increase in hemoglobin to normal values has potential benefits, further research is required to definitively judge whether the possible benefits of hemoglobin normalization may outweigh the negative aspects of increased costs of treatment and possible adverse side effects [3]. The upper limit of the hemoglobin level is set for the elderly, diabetic patients, and patients with high cardiovascular risk (not higher than 12.0 g / dl). In patients on hemodialysis, it is not recommended to exceed a predialysis Hb level > 14.0 g/dl due to the risks of postdialysis hemoconcentration due to ultrafiltration during dialysis [5].

Thus, in the treatment of anemia in such a complex category of patients, there are many unresolved problems and controversial issues. The target values of hemoglobin and the possibility of an individual approach to its level in a particular patient are still the subject of heated discussion. In this regard, it was of some interest to summarize the accumulated experience in the treatment of nephrogenic anemia with Recormon in the two listed dialysis centers, which has more than 1000 patient-years of its use and more than 100,000 injections of

the drug. The aim of the study was a retrospective analysis of the data of more than 5 years of use of the Recormon drug in the Dialysis Center at GKB No. hemodialysis.

Material and Methods

The work was based on examination data of patients who were on program hemodialysis from September 2009 to March 2016 at the Dialysis Center at City Clinical Hospital No. 20. In total, the study included 389 patients, including 192 women and 197 men. The mean age of patients (M+SD) was 52.4+12.2 years (median 53.0 years; 18 to 82 years). The median length of stay on dialysis is 6.5±4.3 years (median 6.1 years; 3 months to 18.5 years). The causes of terminal chronic renal failure (ESRD) were chronic glomerulonephritis (47%), nephrolithiasis and chronic pyelonephritis (12%), polycystic disease (18%), diabetes mellitus (8.6%), hypertensive nephrangiosclerosis (5%) , other established causes (3%), nephropathy of unknown origin (6.4%). Patients underwent hemodialysis according to a standard program (3 times a week for 4–4.5 hours) using Fresenius artificial kidney devices (F4008 S) and using a bicarbonate dialysis solution. The procedure is carried out on individually selected polysulfone dialyzers F6, F7, F8 (all HPS, Fresenius), whose urea clearance in vivo ranged from 196±9.0 to 234±11.0 ml/min, respectively. The blood flow rate is 350±27 ml/min, the flow of dialysate solution is 500 ml/min (in a small part of patients it is 800 ml/min). The delivered dialysis dose (spKT/V index) was > 1.2 (M+SD = 1.34+0.3) according to the logarithmic formula of J. Duagirdas. All hematological analyzes and biochemical tests, including the determination of iron metabolism and the level of endogenous serum EPO, were performed in the independent laboratory "In Vitro". The target value in the Dialysis Center based on the recommendations of EBPG and K/DOQI is Hb > 11 g/dL. In the range of 11–13 g/dl, treatment with maintenance doses of recormon is carried out, except for patients with high cardiovascular risk, for whom the target range is 11–12 g/dl. According to the protocol adopted at the Dialysis Center, Recormon is administered subcutaneously to patients at the end of the dialysis procedure. For statistical analysis, the computerized database of the MedWork Dialysis Center and the Statistica 6.0 software package were used.

Research Results

When patients were recruited after the opening of the Dialysis Center, both primary patients, whose hemodialysis was first started at the Dialysis Center (Group 1), and patients who had already received hemodialysis in other departments (Group 2), were accepted for treatment. The distribution of patients in both groups according to the level of hemoglobin at the beginning of treatment is presented. The median hemoglobin level in group 1 was about 7.7 g/dl, in group 2 it was 8.9 g/dl. Consequently, by the beginning of dialysis, the vast majority of patients had a severe degree of anemia, the severity of which somewhat decreased after being introduced into the dialysis program, which is logically explained by both a decrease in plasma uremic toxicity and the start of therapy with EPO preparations.

Treatment with EPO preparations was started from the first days of the patients' stay in the Dialysis Center. Since 2011, Recormon has been centrally allocated to the Dialysis Center on a regular basis, and since 2012, the need of patients for EPO preparations has been fully satisfied. Since the same year, a convenient dosage form has been used in the form of syringe tubes of 2000 IU of Recormon.

Already 6 months after the start of therapy with EPO preparations, a significant increase in hemoglobin to an average value of 10.2±1.8 g/dl was noted. The effect of the drug in a particular patient clearly depended on the dose. The standard starting dose for a patient weighing 70 kg with severe anemia when administered subcutaneously was 12,000 IU / week, with moderately severe anemia (Hb> 10 g / dl), treatment was started with lower doses (6,000 IU / week). When hemoglobin levels of 10 g/dl were reached, the initial dose (12,000 IU) was reduced by about half, and after reaching the target hemoglobin level, the average doses were 2000–4000 IU/week, or 30 to 60 IU/kg per week.

In 2021, the application of the Dialysis Center for EPO was fully satisfied, which for the first time made it possible to determine the real need for this drug. In 2003, 28814 syringe-tubes containing 2000 IU of recormon were used, while 309 patients were treated during the year, which averaged 3821 IU/week per 1 patient, or 51.2 IU/kg per week. However, in 2021 and 2004 a slight but steady increase in the average values and median of hemoglobin continued - the average hemoglobin content by the middle of 2004 reached 11.4 + 1.4 g/dl, and by the end of it approached 12 g/dl. However, more important, in our opinion, are the qualitative changes observed in our patients. In particular, a greater number of patients reached the target values of hemoglobin (73.4%), the proportion of patients in the highest risk group (Hb <9 g/dl) decreased from 6 to 4%. All this was naturally reflected in a significant increase in the median of hemoglobin and a decrease in the variance of the data

Discussion

Attention is drawn to the fact that patients with ESRD come to the beginning of dialysis with severe anemia. Until recently, the practice of treating nephrogenic anemia in patients already on dialysis has remained unsatisfactory. So, despite the fact that the hemoglobin level in patients of the 2nd group was significantly higher than in the 1st group, it should be noted that the correction of anemia in patients was clearly insufficient, even after several years of hemodialysis, the patients remained deeply anemic, and this practice is all still characteristic of our country. It is noteworthy that the median hemoglobin level in patients at the beginning of dialysis (7.7 g/dL), as well as in patients already receiving dialysis (8.9 g/L), was close to the data of Uzbek Dialysis Society (RDS) published in 2013. However, the problem of insufficient correction of anemia is relevant not only for our country. According to the results of the European Survey Anemia Management (ESAM I) study, only 53% of hemodialysis patients and 40% of peritoneal dialysis patients reached the target Hb level of 11 g/dl. Nevertheless, the percentage of patients with anemia of renal origin in the world is steadily declining, as shown by the results of recent studies ESAM II and DOPPS II. This was largely facilitated by the adoption of the K/DOQI and REPBG recommendations [6–8, 11].

CONCLUSION

Based on our data, as well as numerous publications by other researchers, we can conclude that recormon is an effective and safe drug in the treatment of anemia in patients on program hemodialysis. The effect of the drug is realized at relatively small doses (from 30 to 60 IU/kg), which is significantly less than the declared doses of other EPO drugs approved for use in Uzbekistan. At the same time, subcutaneous injection of epoetin-beta is painless, since, unlike Uzbek generics of epoetin-alpha, recormon does not contain human albumin molecules as a

stabilizer. The undoubted advantage of the drug is the variety of dosage forms and dosages, which makes it possible to individualize the treatment of nephrogenic anemia in a particular patient.

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