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EVALUATION OF HEMODYNAMIC PARAMETERS AFTER TREATMENT OF FUNCTIONAL ANEMIA IN CHILDREN WITH **CHRONIC KIDNEY DISEASE**

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ABSTRACT

This manuscript presents comprehensive treatment for children suffering from functional anemia with chronic kidney disease and evaluates their hemodynamic parameters and cytokine profile. The results of iron metabolism indicators (serum iron, serum ferritin, and transferrin), hemoregulatory hormones (erythropoietin and hepcidin), and pro-inflammatory blood markers (IL-6 and TNF- α) are determined. The therapy method included sucrosomal iron (Sideral) + erythropoietin (Repo) alongside traditional therapy. Thus, an individual approach is necessary for treating functional anemia in patients with varying degrees of chronic kidney disease.

KEYWORDS

Anemia, chronic kidney disease, serum iron, serum ferritin, transferrin, erythropoietin, hepcidin, sucrosomal iron.

INTRODUCTION

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Anemia in chronic kidney disease (CKD) in children is a serious problem requiring a careful and comprehensive treatment approach. Recent years have seen the development and implementation of various therapeutic, diagnostic, and therapeutic-diagnostic measures aimed at eliminating anemia in children with CKD [1-3]. International research recommendations on the diagnosis and treatment of anemia have been summarized in several works (KDOQI, 2006; NICE, 2011; KDIGO, 2012) [4, 5], but some aspects of anemia treatment strategy in children with CKD are covered very briefly. Further study of the features of anemia in children with CKD is needed to optimize treatment [6]. Correcting anemia is the main factor reducing the mortality rate of children with CKD. Clinical use of erythropoiesisstimulating agents (ESAs) in treating anemia in children with CKD helps improve quality of life, appetite, and physical activity tolerance [7].

In the modern world, two main components are effective in treating anemia in children with CKD - iron preparations and erythropoietin [8]. Iron deficiency treatment, through oral or intravenous preparations, reduces anemia severity in CKD patients. Iron deficiency level is one of the main

for decreased sensitivity reasons to erythropoietin therapy [9].

Various modern drugs such as epoetin alpha, epoetin beta, and darbepoetin alpha are used to treat anemia in children with CKD, widely increasing hemoglobin levels in children with CKD [10-12]. For correcting iron in the body, iron preparations are used. These can be oral preparations like iron sulfate or gluconate, or intravenous preparations like iron sucrose [13-16].

It is important to note that anemia in children with chronic kidney disease can negatively affect their growth, physical, and psychological development, making its treatment a relevant problem requiring constant attention and care from medical professionals and parents [17-22].

Thus, the problem of treating anemia in children with chronic kidney disease remains relevant, requiring an individual approach to each patient, comprehensive and timely treatment, and constant health monitoring.

Research Aim: To evaluate the results of iron metabolism parameters (serum iron, ferritin, transferrin), erythropoietin and hepcidin hormones, and blood inflammatory markers after

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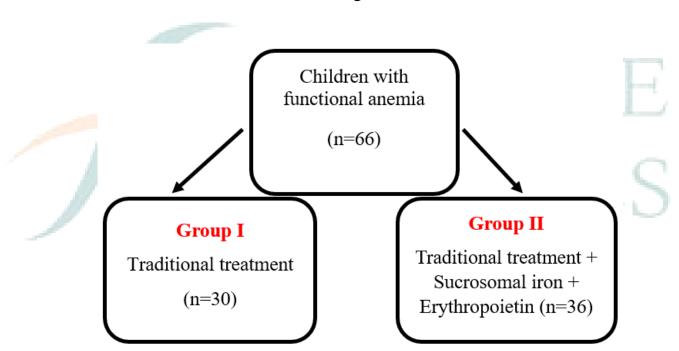
comprehensive therapy in children with functional anemia and chronic kidney disease.

METHODS

Of the 95 examined patients with chronic kidney disease (CKD), 66 children had functional anemia. They were divided into two groups. Group I

included 30 patients (8 children with stage II CKD, 18 with stage III CKD, 4 patients with stage IV CKD) receiving traditional therapy only. Group II included 36 children (7 with stage II CKD, 23 with stage III CKD, and 6 with stage IV CKD) who received comprehensive treatment alongside traditional therapy (Fig.1).

Fig. 1



Therapy for Children with CKD and Functional Anemia Using a Comprehensive Method Lasted for 3 Months. Before initiating erythropoietin therapy, it was necessary to rule out vitamin B12

and folic acid deficiencies, as their lack reduces therapy effectiveness. Iron deficiency also needed to be addressed both before starting erythropoietin treatment and throughout its

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duration. Therefore, Sideral was prescribed from the first day of kidney therapy. After 1 month of taking sucrosomal iron (1 capsule once a day regardless of the time of day and food intake), upon reaching moderate levels of iron and hemoglobin (Fe >6 μ mol/L; Hb >89 g/L), erythropoietin was administered to children. The initial dose was 40 IU/kg body weight subcutaneously twice a week for 4 weeks. Then, the drug was administered subcutaneously once a week for 8 weeks, with the dosage depending on the hemoglobin level in the blood, which was monitored every 10 days. If the hemoglobin increase was adequate (>10 g/L but not exceeding 20 g/L), the erythropoietin dose remained the same. If the hemoglobin increase was inadequate (<10 g/L), the dose was increased by 25%. If the hemoglobin increase exceeded 20 g/L, the erythropoietin dose was reduced by 25%.

Adverse Effects of Epoetin Alpha: Like any medication, epoetin alpha can cause side effects. Although most patients tolerated it well, it is important to be aware of possible adverse reactions such as arterial hypertension, observed in 17% (6) of patients, fever and chills in 15% (5) of patients, local reactions after injection in 10% (3) of children, and headache, dizziness, and

weakness in 36% (10) of patients. Other potential side effects include nausea, vomiting, allergic reactions, and anaphylactic shock, none of which were observed among the patients.

After completing the full course of comprehensive treatment (1 month with Sideral + 3 months with Sideral + erythropoietin), there was a significant improvement in the condition of the examined children. Children in this group developed an appetite, facial blush, weight gain, disappearance of dry skin, brittle nails, dull and thinning hair. They became more energetic, performed better in school, fell ill less often, and were less bothered by symptoms such as headache, dizziness, fatigue, chills, cold extremities, shortness of breath during physical activity, and visual disturbances.

RESULTS AND DISCUSSION

The importance of blood iron parameters should be noted. Serum iron levels after standard treatment were 10.35 ± 0.4 (p <0.05) µmol/L, while after comprehensive therapy, they nearly doubled to 14.36 ± 0.54 (p <0.05) µmol/L, indicating the rapid absorption of sucrosomal iron by the body and an increase in serum iron levels. With the reduced influence of the inflammatory process, serum ferritin normalized

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and reached 104.59 ± 23.86 (p < 0.05) µg/L in Group I patients, whereas in Group II children, it approached optimal values, reaching 93.01±3.71 (p <0.05) µg/L. As serum iron increased, transferrin levels also rose. In Group I children,

traditional treatment results were 2.43±0.1 (p <0.05) g/L, and after comprehensive treatment, levels approached those of healthy children, reaching 2.62 ± 0.04 (p < 0.05) g/L (Table 1).

Table 1. Blood Iron Metabolism Indicators in Children after Treatment **Functional Anemia**

| Indicators | Healthy, | Before | After Treatment | |
|------------------|------------|--------------|-----------------|------------|
| | M±m | Treatment, | Group I, | Group II, |
| | (n=20) | M±m (n=66) | M±m (n=30) | M±m (n=36) |
| Serum iron, | 14,35±2,26 | 7,34±0,31 | 10,35±0,4 | 14,36±0,54 |
| μmol/L | R(|) [| P<0,05 | P<0,05 |
| Ferritin, µg/L | 90,0±18,97 | 131,23±4,07 | 104,59±23,22 | 93,01±3,71 |
| // | | | P<0,05 | P<0,05 |
| Transferrin, g/L | 2,8±0,25 | 2,07±0,08 | 2,43±0,1 | 2,62±0,04 |
| | J | 701 | P<0,05 | P<0,05 |
| Erythropoietin, | 17,8±3,85 | 4,74±0,43 | 11,01±0,71 | 14,36±0,65 |
| mIU/mL | | | P<0,05 | P<0,05 |
| Hepcidin, ng/mL | 40,5±12,49 | 211,16±12,46 | 101,51±11,95 | 72,9±1,89 |
| | | | P<0,05 | P<0,05 |

Note: P - significance of differences between iron metabolism data in blood and indicators before treatment

The erythropoietin (EPO) level after traditional treatment was 11.01 ± 0.71 (p < 0.05) mIU/mL. However, after comprehensive therapy, the EPO level significantly increased threefold, reaching a

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concentration of 14.36 ± 0.65 (p < 0.05) mIU/mL. This demonstrates the positive impact of

comprehensive methods on hematopoiesis and kidney function (Fig. 2).

Fig. 2

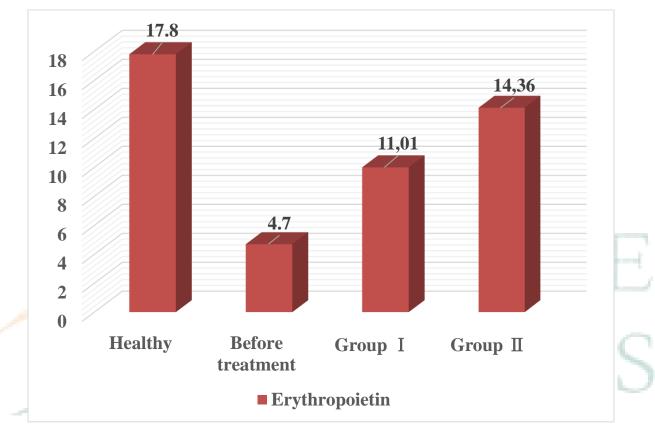


Fig. 2 Results of Erythropoietin Levels after Treatment in Children with Functional Anemia

Hepcidin levels after standard therapy were 101.51 ± 11.95 (p <0.05) ng/mL, but after comprehensive treatment, they significantly decreased by 2.5 times, reaching 72.9 ± 1.89 (p <0.05) ng/mL. This is because anti-anemic drugs and erythropoietin preparations aim to increase

the number of red blood cells and hemoglobin levels in the blood, which in turn reduces hepcidin levels. Lowering hepcidin levels allows for better absorption of iron from food and improves its utilization for red blood cell formation, thereby helping to combat anemia (Fig. 3

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Fig. 3

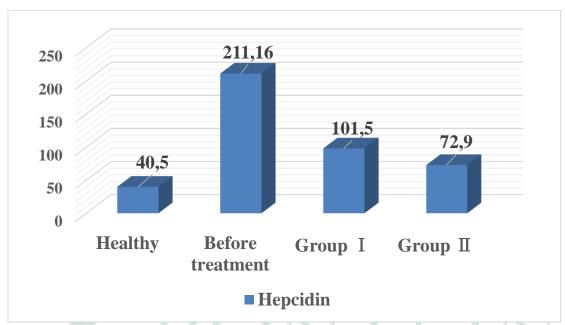


Fig.3 Results of Hepcidin Levels in Functional Anemia after Treatment in Groups

The reduction in inflammatory activity was confirmed by the decrease in IL-6 levels in the blood of Group I to 9.53 ± 0.55 (p < 0.05) pg/mL, while in Group II, its concentration dropped twofold, reaching 7.38 ± 0.24 (p < 0.05) pg/mL. The

concentration of TNF- α in the blood after traditional therapy was 6.82±0.42 (p <0.05) pg/mL, and after comprehensive therapy, it significantly decreased threefold, reaching 4.03±0.15 (p <0.05) pg/mL (Table 2).

Table 2. Cytokine Marker Parameters after Treatment for Functional Anemia

| Indicators | Healthy, M±m | Before | After Treatment | |
|-------------|--------------|------------|-----------------|------------|
| | (n=20) | Treatment, | Group I, | Group II, |
| | | M±m (n=66) | M±m (n=30) | M±m (n=36) |
| IL-6, pg/mL | 5,5±1,42 | 17,03±0,46 | 9,53±0,55 | 7,38±0,24 |
| | | | P<0,05 | P<0,05 |

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| TNF-α, | 2,5±0,47 | 16,61±0,63 | 6,82±0,42 | 4,03±0,15 |
|--------|----------|------------|-----------|-----------|
| pg/mL | | | P<0,05 | P<0,05 |

Note: p - significance of differences between cytokine markers and indicators before treatment

Conclusion

Sideral (sucrosomal iron) combined with Erythropoietin is an effective treatment for functional anemia in chronic kidney disease (CKD). Erythropoietin stimulates the bone marrow to produce red blood cells, thereby improving erythropoiesis. While iron itself does not directly impact kidney function, increasing its levels enhances hemoglobin and red blood cell concentrations, stimulating hematopoiesis and reducing anemia symptoms, as well as improving oxygen supply to kidney tissues. Adequate levels of iron and hemoglobin normalize serum ferritin and transferrin levels in children with functional anemia. The reduction of inflammation (IL-6 and TNF- α in the blood) due to the effective action of comprehensive procedures reduces the load on the kidneys, successfully utilizing hepcidin and lowering its concentration in the blood. The decreased hepcidin level allows for better iron absorption from food and improves its utilization

for red blood cell formation, thus helping to combat anemia.

Therefore, the combined use of Erythropoietin and Sideral corrects functional iron deficiency and prevents anemia development without adverse reactions, thereby improving kidney function.

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