# THE INFLUENCE OF OMAKOR ON THE INDICES OF LIPID METABOLISM IN CHILDREN HAVING GLOMERULONEPHRITIS WITH NEPHRITIC SYNDROME

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**Abstract:** *The aim of the work was to assess effects of Omakor on the indices of lipid metabolism in children having glomerulonephritis with nephritic form (NF) of chronic glomerulonephritis (CGN).*

**Methods:** *examinations were performed on 62 sick children (34 boys and 28 girls) with NF CGN, mean age 11,6±0,17 years, prescription of the disease 4,31=0,31 years. In 13 children there were impaired functions of the kidneys. In the first group 38 children were given standard therapy; 24 children of the second group were given Omakor 1 capsule a day (in the morning after meal) during 15 days against the background of standard therapy. Indicators of the lipid specter were estimated with a biochemical autoanalyzer «Daytona» from Randox.*

**Results:** *inclusion of Omakor in the complex of standard therapy resulted in a reliable decrease of total cholecterol (TCS) in children with the saved and impaired function of kidneys as compared with the initial values the 1,2 and 1,4 times respectively, triglyceride (TG) – 1,24 and 1,23 times, cholesterol of lipoproteins of low density (CS-LPLD) – 1,32 and 1,64 times. The level of cholesterol of very low density lipoproteins (CS VLDL) had a tendency to decrease, cholesterole of high density lipoproteins (CS HDL) to increase. Such alterations in the patients I.ipid specter of blood serum promoted decreased coefficient of atherogenicity to 3,26±0,15 and 3,29±0,83. Conclusions: standard therapy NF CGN fails to substantially influence on dyslipoproteidemia. Inclusion of Omakor in the standard therapy promoted a reliably decreased levels of TG, TCS, CS -VLDL and CS-HDL, and as a consequence, atherogeneity coefficient.*

**Key words:** *chronic glomeru;lonephritis, children, nephritic syndrome, Omakor, lipid metabolism*

## INTRODUCTION

Nephropathies are widespread in pediatric practice and account for 5-7% of common diseases [1]. Chronic glomerulonephritis (CG) is one of the diseases specific to the Central Asian region [2,3], and in many cases is considered one of the causes of end-stage renal failure along with acquired nephropathies. Glomerulonephritis (GN) is the second most common kidney disease in children, behind urinary tract infections. It is the main reason for long-term renal failure (CRF). The most prevalent type of GN is nephrotic syndrome (NS), which drastically lowers ability of organism to adjust [2].

Recent studies have examined the effects of a variety of modifiable and non-modifiable factors on the progression of chronic glomerulonephritis (CGN), with particular focus being placed on the disease's high activity, systemic and intraglomerular hypertension, hyperfiltration, hyperlipidemia, proteinuria, and tubulointerstitial sclerosis [3-5]. Experimental and clinical studies of subsequent years made it possible to deeply study the pathogenesis of CG, that is, as a result of this disease, pathological changes were observed in many tissues and organs. According to some authors [2,4], liver dysfunction leads to changes in metabolism. It should be noted that CG, especially its nephrotic form, is accompanied by impaired lipid metabolism [2]. They are mainly characterized by hypercholesterolemia, hypertriglyceridemia, and this occurs as a result of impaired lipoprotein metabolism in the liver.

Hypercoagulability and severe lipidemia, as manifestations of NS, create real prerequisites for the development of glomerulosclerosis and chronic renal failure [6], which necessitates the search for effective ways to correct these changes. The symptoms characteristic of the nephrotic syndrome of CG are edema and hypercoagulability. Therefore, antihypertensive drugs and anticoagulants are used in medical procedures, which leads to more positive dynamics in elderly patients. A feature of homeostasis in children is that the drugs used sometimes cause complications. Therefore, the development and improvement of new treatment methods is considered one of the urgent problems of pediatric nephrology. In this regard, the drug omakor (Solvay Pharma) is promising, the lipid-lowering effect of which is due to the delay in the synthesis of very low density lipoproteins and the increase in their oxidation in peroxisomes. It contains omega-3, docosahexaenoic and eicosapentoenoic acids, vitamin E. Omacor's capacity to affect platelet aggregation by reducing thromboxane A levels is another advantage. [7,8]. In the literature, we did not find reports on the use of omakor in patients with nephrotic form (NF) of CGN, which served as the basis for this study.

## MATERIALS AND METHODS

62 kids with (34 males and 28 girls) were being watched. The disease lasts 4,31± 0,31 years, and the average patient age is 11,6 ± 0,17 years. A drop in hormone dosage or a modification in the treatment plan caused the condition to recur in 16% of the patients evaluated, an infection in 72% of the patients, and an unknown cause in 4% of the patients. The findings of a thorough clinical and laboratory examination performed at the pediatric nephrology department of the first clinic of the Tashkent Medical Academy served as confirmation for the diagnosis in each case. Kidney function was unaffected in 49 youngsters while it was in 13 others. A diagnosis of illness exacerbation was made. Edema was moderate in 80,6% of the examined children; anasarca was observed in 12 children. Hypoalbuminemia and hyperlipidemia occurred in all patients; 50% had hepatomegaly of varying severity. Taking into account the severity of clinical and laboratory parameters, the patients were distributed as follows: with a severe course, 19 (30,6%); moderate, 43 (69,4%).

All patients received standard pathogenetic therapy, including glucocorticoids, heparin, chime agents, diuretics, and other symptomatic agents. In case of frequently recurring variants of the course, cytostatic drugs were additionally prescribed in generally accepted doses. To assess the effectiveness of omacor, the patients were divided into two comparable groups: 38 patients of the first group received standard therapy; 24 patients of the second group, against the background of standard therapy, took omacor 1 capsule of omacor 1 time per day (in the morning, after meals) for 15 days. The lipid metabolism indices of 20 healthy children of the same age served as the control.

Along with the generally accepted clinical and laboratory studies, the concentrations of total cholesterol (TC), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C) in blood serum were determined in all children on a Daytona biochemical autoanalyzer by Randox. The levels of very low-density lipoprotein cholesterol (VLDL-C) and low-density lipoprotein cholesterol (LINP-C) were obtained by calculation using the generally accepted Friedwald formulas (1972). To determine atherogenicity, the atherogenic coefficient (CA) was calculated, as proposed by A.N. Klimov (1977). Digital material processed by the method of variation statistics.

## RESULTS AHD DISCUSSION

In lipidograms of all patients with NF CGN, an increase in the content of total cholesterol, triglycerides, LDL cholesterol, and VLDL cholesterol was recorded in the blood serum. The severity of these changes depended on the severity of glomerulonephritis and the preservation of kidney function. Thus, the content of total cholesterol in patients with preserved renal function and in patients with signs of renal failure increased statistically significantly by 1,86 and 2 times, respectively (table). More pronounced increases (respectively, 2,46 and 2,55 times, ($P< 0,001$) increased the level of triglycerides. The content of VLDL-C and LDL-C in patients with preserved renal function increased by 2,4 and 2,18 times, and in patients with impaired renal function, by 2,5 and 2,34 times. Along with this, there was a tendency to increase the amount of HDL-C, which was associated with multidirectional changes in this indicator. So, out of 62 children with NF CGN, in 14 this indicator decreased by 1,5–1,3 times, in 42 there was a tendency to increase it, and in the rest it remained within the normative values. A mixed kind of hyperlipidemia was present as a result of these changes, which naturally caused a considerable rise in CA: 2,1 times in patients with normal renal function and 2 times in individuals with impaired renal function. These alterations matched the severity of hyperfibrinogenemia seen in the kids whose blood we looked at.

**Lipid profile parameters in children with NF CGN before and after treatment, X±m**

| Indications | Control group (n=20) | Before treatment ($n_1$=49, $n_2$=7) | After treatment | |
|---|---|---|---|---|
| | | | Standard ($n_1$=31, $n_2$=7) | Standard+omacor ($n_1$=18, $n_2$=6) |
| Total cholesterol, mg/dl | 177,6±8,1 | 329,8±8,3[a]<br>353,9±31,8[a] | 298,3±7,7[a,b]<br>290,1±13,9[a] | 277,2±10,5[a]<br>254,3±3,2[a,b] |
| Triglycerides, mg/dl | 120,9±9,4 | 297,9±8,8[a]<br>307,9±23,3[a] | 268,0±6,4[a]<br>269,4±8,2[a] | 240,4±12,7[a]<br>250,0±14,0[a] |
| Cholesterol-HDLP, mg/dl | 43.5±1.5 | 55,1±1,5[a]<br>61,0±5,2[a] | 59,7±2,9<br>66,1±7,4[a] | 65,9±2,7[a]<br>63,0±9,6[b] |
| Cholesterol-VLDLP, mg/dl | 24,8±1,9 | 59,6±1,7[a]<br>61,6±4,8[a] | 53,6±1,3[a,b]<br>53,9±1,6[a,b] | 48,1±2,5[a,b]<br>50,7±5,1[a,b,v] |
| Cholesterol-LDLP, mg/dl | 98,7±5,6 | 215,1±7,2[a]<br>231,3±27,6[a] | 185,0±7,1[a]<br>170,1±14,3[a] | 163,1±8,9[a]<br>141,3±12,1[a,b] |
| AC | 2,6±0,16 | 5,39±0,24[a]<br>5,22±0,74[a] | 4,57±0,31[a]<br>3,65±0,46[a] | 3,26±0,15[a]<br>3,29±0,83[a] |

Note n1-number of patients with preserved renal function, n2-number of patients with impaired renal function; in the numerator of the values of patients with preserved renal function, in the denominator - with impaired renal function; a-P<0,05 compared to healthy children, b-P<0,05 compared to data before treatment, v-P <0,05 compared with data for patients receiving standard treatment

On the 14th and 15th days of standard therapy, a state of moderate severity with headaches, weakness, swelling on the face, and oliguria were observed in 80,6; 32,3; 51,6; 29; and 19,3% of 31 patients with NF CGN with preserved renal function. Of the 7 patients with impaired renal function, a serious condition persisted in 1, and in the rest it was of moderate severity. All 7 patients complained of weakness, edema on the face and legs (5 patients), and oliguria (3 patients). Despite some improvement in lipidograms, the levels of total cholesterol and triglycerides exceeded the standard values by 1,68 and 2,22 times in children with intact kidney function and by 1,63 and 2,23 times in those with impaired renal function. The content of VLDL-C tended to decrease, while the level of LDL-C decreased statistically significantly by 1,2 and 1,36 times, respectively. The concentration of HDL-C did not change significantly. CA remained high, amounting to 4,57 0,31 and 3,65 0,46, respectively.

Therefore, it can be said that the standard therapy of CGN NF does not have a corrective effect on the lipid spectrum of blood serum, which is manifested by the preservation of high values of all cholesterol fractions, TG and CA levels. This dictates the need for the use of lipid-lowering drugs.

Indeed, taking one Omakor capsule per day after meals in combination with standard therapy pronouncedly reduced the level of cholesterol and triglycerides. So, in groups of

sick children with preserved and impaired renal function, the content of OXC significantly decreased relative to baseline values, respectively, by 1,2 and 1,4 times, TG—by 1,24 and 1,23 times, and LDL-C—by 1,32 and 1,64 times. VLDL-C levels tended to fall while HDL-XC levels rose. Such changes in the lipid spectrum of the blood serum of patients led to a decrease in CA to 3,26 0,15 and 3,29 0,83. There was a clear trend towards a decrease in the concentration of total cholesterol, cholesterol in very low and low density lipoproteins, and TG in the blood serum compared with the indicators of children who received standard treatment. Apparently, taking omacor for 15 days is not enough; for a more pronounced correction of lipid metabolism in children with NF CGN, it is advisable to administer it for 1-2 months. Omacor did not significantly affect the clinical symptoms of the disease. Of the 24 patients, the state of moderate severity was noted in 16 (66,7%); headache, weakness, facial edema, and oliguria persisted in 16,7; 37,5; 20,8; and 25% of patients, which generally corresponds to the indicators of patients who received standard therapy.

Lipid metabolism disorders in patients with kidney disease have been repeatedly discussed in the literature. Most often, hyperlipidemia is considered a secondary disorder resulting from changes in the filtration function of the kidneys, a defect in the functions of the tubular epithelium, or interstitial lipid metabolism in the kidneys. At the same time, an increase in the level of total cholesterol and TG corresponds to the severity of the clinical course; it is more pronounced in nephrotic syndrome, which may be associated with the progression of atherogenic processes [9]. A pronounced increase in the content of TG and VLDL in patients with NF CGN is mainly due to increased TG synthesis in the liver and their secretion as part of VLDL. On the other hand, low activity of lipoprotein lipase slows down the utilization of VLDL and LDL, which contributes to their accumulation in the blood.

Normally, LDL binds to receptors and is taken up by cells; are included in lysosomes, where proteins are destroyed, and released cholesterol inhibits the activity of hydroxymethylglutary l-CoA reductase, the main enzyme of cholesterol synthesis [10]. With a deficiency of receptors, the activity of this enzyme is not suppressed, which leads to an increased synthesis of cholesterol. At the same time, type II hyperlipoproteinemia develops, which is characteristic of NS, in which high values of TG, total cholesterol, VLDL-C and LDL-C are recorded.

According to the literature [10], renal disease causes a drop in HDL-C levels. Only a small percentage of the patients had a drop in it, though, and this sign was generally on the rise. An rise in HDL-C levels is a positive development when viewed from the perspective of anti-atherogenicity. E.V. Kolmakova (1990) asserted that chronic renal disorders hinder HDL elimination and/or catabolism. It should be noted that lecithin-cholesterol-acyltransferase activity found in HDL proteins catalyzes the esterification of free cholesterol, mitigating its atherogenic effects. However, despite the preservation of standard values of HDL-C and relatively high levels of total cholesterol, cholesterol-LDL,

and LDL-C in patients with NF CGN, it is not able to neutralize them, which, apparently, determines the increase in CA in our patients.

The pharmacotherapy of dyslipoproteinemia is quite complex and diverse, especially in patients with kidney damage. The main categories of lipid-lowering medications are divided based on their mode of action: 1) Drugs that prevent the absorption of cholesterol from the intestine (bile acid sequestrants and enterosorbents); 2) Drugs that enhance the catabolism of triglycerides (fibrates); 3) Drugs that enhance lipid metabolism at the cellular level (statins); 4) Drugs that reduce the production of LDL and VLDL (nicotinic acid derivatives and omega-3-polyunsaturated fatty acids — PUFA); 5) In recent years, omega-3 polyunsaturated fatty acids, in particular omacor, have been widely used to correct dyslipoproteinemia [3,5]. They are used for the prevention and complex treatment of various pathological conditions manifested by dyslipoproteinemia. PUFAs 0–3 modify HDL, affecting the fluidity of their lipids and the movement of cholesterol into these particles, as a result of which the removal of cholesterol from the cell is facilitated and an antiatherogenic effect is realized. It reduces the synthesis of chylomicrons in the intestine, facilitates their contact with lipoprotein lipase, reduces the synthesis of triglycerides in the liver, and promotes the release of VLDL from the liver into the bloodstream.

Research by T.S. Voznesenskaya et al. (2003) showed the effectiveness of including F-3 PUFA at a dose of 3-4,5 g/day in the standard treatment of nephrotic syndrome in children. Within a month, there was a significant decrease in the levels of cholesterol, triglycerides, and cholesterol-LDL and an increase in the levels of cholesterol-HDL. The inclusion of PUFA c-3 in the diet of children with chronic renal failure at the rate of 3–7 g per day for 2 months led to a decrease in the level of thromboxane B2 and TG in the blood serum and an increase in bleeding time [11]. Omakor appears to improve the rheological characteristics of the blood by reducing platelet aggregation activity, which favorably influences the pathology's course. Due to an increase in the synthesis of anti-inflammatory eicosanoids, a decrease in the production of pro-inflammatory cytokines, and a reduction in the production of platelet aggregation factor, omecor also has an anti-inflammatory impact.

Conclusion

1. CG NF in children is characterized by drastic changes in fat metabolism, especially cholesterol metabolism, and the degree of these changes depends on the severity of the disease and the involvement of the liver in the pathological process.

2. In children with NF CGN, as a result of a violation of lipid metabolism in the blood serum, an "atherogenic type" of hyperlipoproteinemia is established, characterized by a high content of total cholesterol, triglycerides, VLDL-C, and LDL-C against the background of less pronounced changes in HDL-C, which is more typical for patients with impaired renal function.

3. Standard therapy for NF CGN does not have a significant effect on dyslipoproteinemia. The inclusion of Omacor in standard therapy (1 capsule, 1 time per

day for 15 days) contributes to a significant decrease in the levels of TG, total cholesterol, VLDL-C, and LDL-C and, as a result, the atherogenic coefficient.

4. Omacor should be prescribed for a longer period of time, since we did not observe any side effects of the drug. Its inclusion in the complex therapy of NF CGN for the correction of dyslipoproteinemia seems appropriate.

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