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POLYMORPHISM OF THE CYP2C19 ISOENZYME AS A RISK FACTOR FOR GASTROPATHIES INDUCED BY THE USE OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS IN PATIENTS WITH PAIN SYNDROME

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ABSTRACT

In the last decade, there has been a sharp increase in chronic kidney diseases (CKD) among children. In the US, Europe, Australia, Asian countries, it is noted that one-tenth of the world's population suffers from a violation of kidney function. In 50% of patients with SBK, the disease is detected at the 3-5 stage of chronic renal failure (CRF), in 10% of patients at the terminal stage. At present, insufficient research has been conducted in the country to study the features and complications of kidney disease in children (Umarov R.Kh. 2010; Sharipov A.M. 2012; Khamzaev K.A., 2019; Rakhmonova L.K. 2020; Karimova U.N., 2020;).

Key words: children, nephrotic syndrome, glucocorticosteroids.

INTRODUCTION

Nephrotic syndrome in children is characterized by proteinuria > 3,0 g/Day (>50 mg/kg of body weight per day or >40 mg/m^2 of body surface per hour), a decrease in the concentration of albumin in the blood < 25 g/l, the development of hyperlipidemia and tumors [1,2,3,5]. According to A.A. Baranov's data (2018), the annual incidence of nephrotic syndrome accounts for 2-7 primary cases per 100 000 children, while the prevalence rate in children – 12-16 cases per 100 000 children population. [4-7] Tsigin I.A., Komarov O.V. at al (2017) state that every 100 000 children under the age of 10 with primary nephrotic syndrome 2-13 years of age are eligible for the condition. NS in children is about 10% in children under 90 years of age, and in older children about 50%. The congenital form of nephrotic

syndrome is in the ratio of 0,9-1,2 incidence in every 10 000 newborns, this form is common in European countries, especially in Finland. [6-8,19,20]

New approaches to the nephrotic syndrome in children have shown that in recent decades, the results of the treatment of nephrotic syndrome due to the change in ideas about the etiology, pathogenesis and treatment tactics of nephrotic syndrome, the emergence of new therapeutic technologies, sung has shown that there are profound changes in other organs and systems, in particular, the digestive tract. Ignatova M.S., Dlin V.V. (2017). [3-6]

Glucocorticosteroids (GKS) are the main selective preparations used in the treatment of steroid-sensitive nephrotic syndrome (SSNS) in children. Approximately 40% of them would have died before the use of GKS and antibiotics [3]. In 80-90% of patients receiving GKS, ida occurs in the remission phase of the disease[1]. Depending on the response to GKS therapy, SSNS and steroid-resistant nephrotic syndrome (SRNS) are allocated [2].

According to the recommendations of international and Russian scientists, for the treatment of nephrotic syndrome, prednisolone is prescribed to drink at a dose of 60 mg/m^2 per day or 2 mg/kg per day (the dose is 60 mg per day.for 4-6 weeks, then the drug is recommended to take for 4-6 weeks at a dose of 40 mg/m^2 or 1.5 mg/kg (maximum one-day to 40 mg dose), a gradual reduction and a scheme of cancellation of the drug is recommended [1-4]. The total duration of GKS therapy is 4-5 months [7,16].

GKS is an alternative mode of admission, which increases the duration of remission compared to the intermittent mode of admission (continuous) [4-6,16]. Children with frequent recurrent (SSNS) and steroid - dependent nephrotic syndrome (FRNS), which are considered clinical variants of SRNS, need long-term GKS therapy, [9-15]. this leads to serious side effects, including damage to the mucous membranes of the stomach and duodenum [5-8]. Proceeding from the above, it is topical to determine the dependence of clinical-morphofunctional changes in gastroduodenal foci on long-term GKS therapy in children with nephrotic syndrome.

The purpose of the study: in children who have long received GKS therapy with nephrotic syndrome, the study is to investigate the clinical changes observed by the gastrointestinal tract.

Research materials and methods

Under our observation, the indicators in the form of dyspeptic complaints observed in children who received and did not receive GCS for 6 months before admission were analyzed in the multidisciplinary clinic of the Tashkent Medical Academy under the supervision of the Department of Nephrology in the period

from 2018 to 2020. Various clinical variants of nephrotic syndrome were analyzed in the medical documentation (history of the disease) of 298 children aged 4 to 14 years of age.

Results of the study.

According to the results of the analysis, it was found that despetic complaints and signs were observed in 244 (81,9%) children. These children were divided into groups of patients who received GKS for 6 months before hospitalization in 1-Group n=176 (72,1%) hospital hospitalization in two groups and who did not receive GKS within 6 months before hospitalization in 2-Group N=68 (27,9%) hospital. Based on clinical laboratory variants of nephrotic syndrome, it was divided into 3 groups. With the diagnosis of steroid-sensitive nephrotic syndrome (SSNS), in which 1-group was identified as primary and treated with GCS for 12 weeks and achieved remission, children were treated with 64 (26.2%), 2-group were treated with 86 (35.2%), 3-group prednisolone with a diagnosis of frequent recurrence (FR), which is considered a clinical variant of steroid-resistant nephrotic syndrome (SRNS), patients with steroid-dependent nephrotic syndrome (SDNS), which did not achieve remission after a course of weeks of treatment with Sung and 3 times a course of Solu-medrol, received 94 units (38,6%). it was.1-table. Most of the children were hospitalized several times.

Table 1

Clinical description of children with nephrotic syndrome who received and did not receive glucocorticosteroids for 6 months before hospitalization.

Clinical variants of NS	1-group (***n*** = 176)		2- group (***n*** = 68)		P
	abs	%	abs	%	
SSNS=64	3	1,8	61	89,7	P< 0,01
SRNS or FRNS=86	79	44,8	7	10,3	P< 0,02
SDNS=94	94	53,4	0	0	-

Note: against the background of taking 1-group-maximal GKS dose, 2-group-during the most long-term remission of the disease, P-mail data reliability.

In the results of the analysis, 244 patients with dyspnea complaints and signs were analyzed according to age and sex of the children. The age of the children was divided into three age groups, taking into account the critical periods.

The first age group ranged from 4 years to 7 years of age 62 (25,4%), the second age group from 7 years to 10 years 95 (38,9%), the third age group ranged from 10 years to 14 years 87(35,6%), the average age of children was 8,8 ±1,3. P< 0,05.

Table 2

Description of the age and sex of sick children with NS diagnosis

Age	4-7 years (n=62)		7-10 years (n=95)		10-14 years (n=87)		P
Sex	абс	%	абс	%	абс	%	
Girls	18	29,0	26	27,3	38	43,6	P< 0,01
Boys	44	71,0	69	72,7	49	56,4	P< 0,01

Note: P-data reliability.

The results of the analysis showed that dyspeptic complaints and symptoms in children with NS were more common in boys when they were distributed by gender in all age groups than girls, which was generally consistent with the results of the study of many authors. [2-8]. When the social origin of the sick children was pushed, the rural population accounted for a large part (131 (74.3%) in the 1st Group and 54 (79.4%) in the 2nd Group, respectively. Data on the duration of the disease were as follows: 8 years from the onset of the disease in the 1st Group, an average of 5,1±1,8 years; in the 2nd Group-3 years, an average of 1,6±0,6 years. According to the results of the analysis, in isolated groups based on clinical laboratory variants of nephrotic syndrome, dyspnea complaints (pain in the abdomen, vomiting, constipation) were the same.

Table 3

Dyspeptic complaints in children with nephrotic syndrome (pain in the abdomen, vomiting, constipation).

Dispatch complaints	SSNS 1-group (***n=64)***	SRNS or FRNS 2-group (***n=86)***	SDNS 3-group (***n=94)***	**P**
Abdominal pain abs. (%)	11(17,1%)	71(82,5%)	82(87,2%)	P< 0,01
Vomiting abs (%)	13(20,3%)	68(79,0%)	78(82,9%)	P< 0,02
constipation abs. (%)	23(35,95)	54(62,7%)	67(71,1%)	P< 0,01

Note: P-data reliability.

Also, as a result of retrospective studies of the history of the disease, dyspeptic complaints were analyzed in children with nephrotic syndrome who received and did not receive glucocorticosteroids for 6 months before hospitalization. In the 1-group 153 (86,9%) suffered with abdominal pain, vomiting 146 (82,9%), constipation 121 (68,7%) cases. Dyspeptic complaints among patients who did not receive GKS for 6 months or more before 2nd group

hospitalization were identified 11 (16,1%), vomiting 13 (19,1%), constipation 23 (33,8%), abdominal pain. In the 1st group, compared that then the 2nd group dyspeptic complaints vomiting abdominal pain, constipation was detected a lot, it corresponded to the data of the literature. [6-8].

Table 4

Dyspeptic complaints in children with nephrotic syndrome who received and did not receive glucocorticosteroids for 6 months before hospitalization.

Index	Group 1 (n = 176)	Group 2 (n = 68)	P
Abdominal pain	153(86,9%)	11(16,1%)	P <0,01
Vomiting	146(82,9%)	13(19,1%)	P <0,02
Constipation	121(68,7%)	23(33,8%)	P <0,02

Note: 1 — group-against the background of taking the maximum dose of GKS, 2-group-during the most prolonged remission of the disease. P-reliability of data.

CONCLUSION

Dyspeptic complaints (pain in the abdomen, diarrhea, vomiting) were noted in 81,9% of patients who received glucocorticosteroids for a continuous 6 months in nephrotic syndrome, dyspeptic complaints were observed in 18,1% of children who received glucocorticosteroids for less than 6 months, and morphofunctional changes in the intestinal tract of the stomach were associated with the duration and continuaqtion. In the period of remission of the disease in children with a frequent recurrent form of nephrotic syndrome and sensitive to steroids, there was a significant decrease in the incidence of dyspeptic complaints (pain in the abdomen, diarrhea, vomiting), discontinuation of glucocorticosteroid drugs.

Predicting the effect on the state of the gastrointestinal tract in children with nephrotic syndrome, taking different courses of glucocorticosteroids, requires timely diagnosis and treatment of changes.

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