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THE EFFECT OF FOOD DYES ON THE DEVELOPMENT OF KIDNEY DISEASES IN CHILDREN

Z. S. Azimova
Assistant of the Bukhara State Medical Institute Named after Abu Ali Ibn Sino, Bukhara

Annotation*: Children's morbidity diseases of the urinary system occupy second place after respiratory pathology [1]. The increase in the incidence of nephropathies, the increase in primary chronic variants of the course, causes concern and indicates the need for further study of the etiology, mechanisms of development and progression of kidney diseases [2]. To date, the problem of the origin of nephropathies in children remains relevant. The existence of a wide variety of causes leading to the occurrence of nephropathies makes it difficult to decide on the choice of adequate etiotropic and pathogenetic therapy, assessment of the effectiveness of treatment methods [3, 4]. The food coloring agent tartrazine (E 102) was chosen as a food factor, which is widely used in the production of beverages, ice cream, confectionery products. Special susceptibility to tartrazine, in particular, irritability, hyperactivity, restless sleep, was revealed in children [5].*

Keywords: *food dyes, kidney diseases, tartrazine.*

The purpose of the study: to improve the diagnosis and prognosis of the risk of development and progression of nephropathies based on an in-depth clinical and experimental study of the role of phospholipid metabolism under the action of food dyes.

Materials and methods of research: The experiment was conducted on female and male rats. Female rats received 1 ml of 0.1% tartrazine solution (in doses permitted by standards for use in the food industry) for 1 month. The rats were kept in standard vivarium conditions. Part of the rats (7 females of the main and 7 females of the control groups) were hooked to males. During pregnancy and offspring feeding, females continued to receive tartrazine. Some of the descendants of rats were removed from the experiment at the age of 1 month (equivalent to childhood), some at the age of 2 months (equivalent to adolescence). 1-month-old baby rats received tartrazine only through the placenta in utero and with mother's milk, and 2-month-old baby rats were additionally injected with tartrazine intragastrically for 1 month at the same dose as their mothers.

Control groups – intact animals of the same age – received 1 ml of saline solution. In the blood serum of rats, the content of lipid peroxidation products (POL) - malondialdehyde (MDA) and diene conjugates (DC) was determined by spectrophotometric method; the protein composition of blood serum was determined by turbodimetric method; the level of medium–mass molecules (MSM) - by spectrophotometric method; urea, creatinine and aminotransferase activity -; catalase activity – by spectrophotometric method; content of total protein in renal tissue homogenates - spectrophotometric ally, lipids (triglycerides, cholesterol, phospholipids, total lipids) The material for morphological examination — the right kidney, after fixation in 10% formalin, was poured into paraffin wax, and sections 5-6 microns thick were painted with picrofuxin according to Van Giese, a CHIC reaction was performed to clearly identify the basement membranes of glomerular capillaries. Light microscopy was performed using microscopes. We examined 24 children aged 1 to 18 years, of them with glomerulopathy -15

people, with chronic pyelonephritis -14 children. The verification of diagnoses was carried out on the basis of a thorough clinical, laboratory and instrumental examination of patients according to generally accepted methods.

In the group of children with glomerulopathies, there were more older children, boys by gender. In the group of children with pyelonephritis, the ratio of boys/girls depended on the age group (with increasing age of patients, the percentage of girls increased). The structure of pyelonephritis exceeded secondary pyelonephritis against the background of congenital abnormalities of the urinary system, vesicoureteral reflux, neurogenic dysfunction of the bladder, metabolic disorders. It should be noted that often even a thorough analysis of anamnestic data (heredity, pregnancy course) to identify possible causes (genetic, biological, physical, chemical, etc.) of the development of congenital kidney and urinary tract defects did not allow identifying the cause of their development in children. The above allows us to assume that such reasons may be food products containing certain dyes and stabilizers. By means of a questionnaire, the frequency of children's consumption of products containing tartrazine was revealed. At the same time, children with glomerulopathy used tartrazine 2 times more often than children with pyelonephritis.

Phospholipid metabolism (total phospholipids, lysophosphotidincholine, sphingomyelin, phosphatidylcholine, phosphatidylinositide, phosphatidylethanolamine, phosphatidyl acid, phosphatidylserine), the content of glycosaminoglycans in urine, and cholesterol levels were determined in the blood serum of children.

All the digital data obtained were processed by statistical research methods.

Results of the study: As a result of an experimental study in the blood serum of 1-month-old offspring of the main group, compared with the control group, the level of β-globulins was increased with a significant decrease in the level of albumins, which can be regarded as a nephrotic type of proteinogram.

In addition, an increase in the value of the gamma-globulin fraction was found in the rats of the main group, which may be associated with the activation of the humoral link of immunity. Receiving tartrazine in utero and with mother's milk by 1-month-old offspring contributes to an increase in the FAS ligand in blood serum. Continued use of tartrazine by 2-month-old offspring showed an increase in the FAS ligand, especially in males. This fact, together with the fact of an increase in the gamma-globulin fraction of proteins, can be regarded as the presence of an autoimmune process.

An increase in creatinine and blood urea with prolonged use of tartrazine in rats of the main group compared with the control can be considered as criteria for functional disorders in the kidneys. That the longer the animal uses tartrazine, the more pronounced the functional disorders in the kidneys. At the same time, the increase in urea and creatinine levels in males is greater than in females.

In 1-month-old males of the main group, the activity of AsAt and AlAt was increased, the content of total protein was reduced, the level of lipids was increased (mainly due to triglycerides, with a decrease in the content of phospholipids).

In females, the activity of AsAT and AlAT was increased with an increased protein content relative to the control group (Table 2). The content of total lipids does not differ from the level in control animals, but the serum content of phospholipids is reduced, and triglycerides are increased.

In males, the processes of SEX were activated (the content of MDA and DC increased) with a decrease in the activity of the antioxidant system (catalase activity decreased). In females, catalase activity does not differ from the level of catalase in control animals.

In males, sexual processes were activated (the content of MDA and DC increased) with a decrease in the activity of the antioxidant system (catalase activity decreased). In females, catalase activity does not differ from the level of catalase in control animals.

It is known that the degree of toxicity of a substance that is injected into the body can be estimated by the content of medium-weight molecules. The study of this indicator in blood serum showed that the level of MSM is on average 2 times higher than in animals of the control group. As can be seen, the toxic load leads to the activation of POL processes, the activity of AOS enzymes increases compensatorily. In males of the main group, the content of SEX products is lower than in the control group, and the activity of AOS enzymes does not differ from the control group.

The study of the lipid content in renal tissue homogenates showed that in males and females of the main group, the level of phospholipids was reduced with an increased cholesterol content, which may be associated with a violation of the level of transport forms of lipids in the blood. A decrease in the level of phospholipids may be the reason for the renewal of the phospholipid component of the membranes and, in this regard, with a change in the transport of nephrocytes through the membranes and regulatory processes in the renal tissue.

Thus, the results obtained allow us to assume that in 1-month-old animals of the main group, especially in males, there is an imbalance in the SEX system and antioxidant activity in the kidneys, which indicates violations in the course of metabolic processes in general. Males and females also have disorders in the synthesis and content of lipids. Probably, the decrease in the level of phospholipids is associated with the development of ant phospholipid antibodies (an autoimmune process). Analysis of the results of the study of 2-month-old offspring rats who received tartrazine in utero, with mother's milk, and after switching to self-nutrition for 1 month they independently consumed tartrazine with food, indicates that these animals have impaired metabolic processes in the kidneys: the level of phospholipids is reduced with elevated cholesterol levels. Changes in metabolic processes lead to functional disorders, as evidenced by an increase in the level of creatinine and urea in the blood of animals of the main group. At the same time, the longer the animal receives tartrazine, the more pronounced the metabolic and functional disorders on the part of the kidneys. Based on the data of biochemical studies, it can be assumed that in males who received tartrazine, renal dysfunction is more pronounced than in females. Morphologically, in 1-month-old rats treated with tartrazine in utero and with mother's milk, the glomeruli of the kidneys are placed unevenly in the cortex. A significant part of the glomeruli are reduced, represented by a small number of capillaries. Normally developed glomeruli function with increased load, they are hypertrophied. The appearance of Ig G and an increase in the number of macrophages in some glomeruli indicates the formation of immune damage and inflammation of the glomeruli. The morphological picture of the lesion of the epithelium of the tubules, in places with clusters of macrophages in the stroma may indicate the beginning of the development of tubulo-interstitial nephritis.

If an individual with an intrauterine onset of tartrazine intake into the body continues to receive it after birth, the active glomeruli look hypertrophied. At the same time, a large number of macrophages are detected in them, active fibroblasts are found, and the process of sclerosis of both the capillary wall and the mesangium is intensively underway. Thus, the rat’s equivalent to the “adolescent” age has histological signs of chronic glomerulonephritis. A significant lesion of

the tubule epithelium with the accumulation of macrophages in the interstitial and sclerosis of the arteriole wall can be interpreted as signs of chronic tubulo-interstitial nephritis.

The results of the clinical study showed that the most significant changes in the phospholipid composition of blood in children are observed in patients with glomerulonephritis (especially with nephrotic syndrome) who received products containing tartrazine more often than several times a month. There was a significant increase in the levels of lysophosphatidylcholine (96.5±7.4 mg/l) and phosphatidylinositide (73.5±11.6 mg/l), a more significant decrease in the levels of negatively charged phospholipids (phosphatidylcholine - 254.3±12.9 mg/l, sphingomyelin - 177.2±21.5 mg/l) in children with glomerulonephritis compared with patients with pyelonephritis (64.5±16.7 mg/l; 50.6±20.1 mg/l; 322.4±17.5 mg/l; 180.8±12.8 mg/l, respectively).

The absence of reliable changes in the concentrations of other phospholipid fractions may be due to the possibility of their mutual conversion, the speed of plastic processes of the child's body. Changes in the phospholipid spectrum of blood in children with pyelonephritis depended on the degree of inflammation activity, the involvement of interstitial tissue in it, and the functional state of the kidneys. The results of the study indicate the presence of membrane disorders that depend on the severity of the disease and the activity of inflammation in glomerulonephritis and pyelonephritis. A study of the content of total phospholipids in urine showed that their level increases significantly with nephrotic glomerulonephritis syndrome. There was a significant difference in the levels of glycosaminoglycans in urine – with glomerulonephritis (88.3 ± 16 mmol/l), their level is almost 1.5 times higher than with pyelonephritis (52.1± 9.3 mmol/l). These changes may indicate not only the severity of membrane disorders in glomerulonephritis, but also give rise to the assumption that connective tissue dysfunction is important in the development of this pathology, the clinical manifestations of which revealed signs of connective tissue dysplasia.

According to the data obtained, there are significant differences in the content of urine GAG, LPH and blood PHI in children with glomerulonephritis and pyelonephritis, which indicates the most pronounced processes of destabilization of cell membranes and connective tissue in children with glomerulonephritis. Analysis of the obtained data revealed the presence of significant positive correlations between blood cholesterol levels and LPH ($r=0.49$, $p<0.05$), PHI ($r=0.74$, $p<0.05$), levels of total blood PH and PHI ($r=0.65$, $p<0.05$), LPH and PHI in children ($r=0.49$, $p<0.05$). Negative correlations were also found between the levels of urine GAG and total blood PH ($r=-0.47$, $p<0.05$), LPH and blood PH ($r=-0.62$, $p<0.05$).

The revealed changes in the phospholipid composition of the blood, the levels of glycosaminoglycans in urine in children with glomerulonephritis and pyelonephritis, unidirectional correlations between a numbers of indicators suggest that tubular disorders may occur in the genesis of these changes, as a factor of activity and severity of the inflammatory process. In addition, changes in the indicators of destabilization of cell membranes can be influenced not only by the activity of inflammation, the involvement of tubulo-interstitial tissue in the pathological process, but also by the combined action of various factors, including food, which is confirmed by experimental research.

Conclusions: 1. Based on the results of the study, it can be assumed that the influence of nutritional factors acting on a person throughout life act as toxic and xenobiotic agents that cause damage to both the glomeruli of the kidney and the tubular epithelium, which leads to the deployment of more intensive (but incomplete) regeneration of the kidneys with a decrease in their functionality. 2. The intrauterine onset of damaging factors greatly aggravates the negative

impact, since during the period of embryophetogenesis, there is a violation of the formation of renal structures. 3. Synthetic food additives in modern living conditions are a risk factor for the development of nephropathies in children.

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