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PRINCIPLE OF TREATMENT OF CHRONIC TUBULOINTERSTITIAL NEPHRITIS IN CHILDREN

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Relevance. Advances in the diagnosis and treatment of nephrological diseases in children are colossal, but nevertheless, in about 23% of patients the disease has a progressive course, which significantly affects the formation of quality of life. The interstitial tissue of the kidneys is the focus of pathology in TIPP, further covering the blood vessels, lymphatic vessels and tubules of the renal stroma [5;7].Despite the successes achieved in the treatment and prevention of CTIN in children,Currently, there is no exact algorithm for diagnosing this pathology in the literature. Comparative clinical and laboratory diagnostics of the main types of tubulointerstitial nephritis is also not fully developed. There is no data on the pathogenetic relationship between tubular functions and indicators of protein metabolism in blood serum and urine in children with different forms of CTIN. The development of a new pathogenetically substantiated complex treatment for CTIN in children remains a significant research task [8;9].

Purpose of the study. To develop a method for complex correction of CTIN in children, taking into account the pathogenetic significance of protein metabolism parameters, endogenous intoxication and disorders of tubular functions.

Materials and methods of research. This study presents the results of examination and treatment of 120 children with CTIN, in the phase of active inflammatory process, who were in the children's nephrology department of the Children's Regional Multidisciplinary Scientific Center in Samarkand, in the period from 2019-2021.

Taking into account the clinical variant of CTIN, all patients were divided into 2 groups: group 1a - 51 (43%) children with a recurrent form of CTIN and group 2 - 69 (57%) patients with latent CTIN. Among them there were 65 boys (54%), 55 girls

(46%). The patients underwent general clinical, laboratory and instrumental examinations.

The clinical diagnosis of CTIN was made according to the diagnostic criteria proposed in the classification of N.A. Korovina (2003), where special attention was paid to the characteristics of the pedigree history: determination of IMS, TIN, ICD, metabolic disorders at an early age, which were symptoms of exudative-catarrhal diathesis, dysuric disorders against the background of crystalluria.

"Urinary syndrome" was characterized by: abacterial leukocyturia, high osmotic density of urine, microproteinuria, microhematuria, crystalluria.

The control group consisted of 30 practically healthy children who did not suffer from chronic diseases, who had not been ill for the last 6 months, with a favorable nephrological family history, aged from 4 to 15 years. Renal parameters were assessed during the period of exacerbation of the disease, during the formation of clinical and laboratory remission, 1 year, 2 and 3 years after the period of exacerbation. The study did not detect children with CTIN due to severe congenital pathology in combination with impaired renal function.

The state of renal functions was assessed based on two groups of functional techniques:

Group I - methods indicating the quantitative state of the renal functions of various parts of the nephron.

a) The state of renal filtration function (endogenous creatinine clearance) was assessed using the Van Slyke formula:

Cystatin C was determined using immunotubidimetry using a Cobas Integra 400 plus device (Roche, Switzerland):

– this is a protein that is formed at a constant rate in the nucleus of cells;

– has the property of free filtration in the glomeruli;

– inversely correlates with GFR and is highly sensitive to its changes compared to its changes in creatinine [9].

– during the process of reabsorption, it is metabolized in the proximal tubules

– is formed regardless of gender, body weight or tumors, the presence of inflammatory processes;

To determine the concentration ability of the kidneys, the Zimnitsky test was used. In addition, the magnitude of ammonia acidogenesis was determined (titratable acids and ammonia were determined in daily urine).

In all examined patients, blood protein levels were determined.

Serum creatinine and urea levels were also determined.

The results obtained and their discussion: The clinical group (group 1: 52 patients) with rCTIN was identified based on the presence of typical signs of the disease, such

as dysuria (32.7%), neurogenic bladder (10%), pasty soft tissue of the eyelids in the morning (46.5%), lower back pain (30.8%) due to physical activity (26.9%).

Whereas, the clinical group (group 2: 68 patients) with lCTIN was identified on the basis of a more permanent symptom of “salt-losing kidney”, which leads to the development of muscle hypotension - 41.2% (28) and arterial hypotension - 27.9% (19), dysuria - polyuria in 54.4% (37) of patients, the presence of abacterial damage to the renal tissue against the background of hyperoxaluria - 100% (68), abundance of epithelium in 92.6% (63), cells of a lymphomonocytic nature - 88.2 % (60), brown cylinders - 100% (68). Urine cultures are sterile.

In the clinical status of patients with a chronic recurrent course of TIN, the frequency of exacerbation of the disease over the past period was determined and revealed that in 19 (37.7%) children the frequency of exacerbation was 1 time per year, in 20 (37.5%) children 2 times per year and in 13 (24.1%) children more than twice a year.

The data obtained showed that the concentration of MPP in the urine in patients with rCTIN in the acute phase was 16.3 times higher than the control group (Fig. 1), while in children with lCTIN it was 8 times higher. More pronounced disturbances in cellular structures were noted in patients with rCTIN compared to patients with lCTIN.

An increase in the level of MPP in urine in CTIN is apparently due to the fact that during inflammatory-destructive processes of the tubulointerstitial system, the reabsorption of MPP in the proximal tubules is disrupted, since they are reabsorbed there by 99.9%, as a result of which their excretion in the urine is observed. The accumulation of MPN in urine is facilitated by impaired excretory function of the kidneys, leading to tubular atrophy and organic structural disorders.

In our opinion, the identified changes are associated with more active intoxication that persists for a long time, which is the cause of excessive accumulation of toxic substances that contribute to the formation of endotoxicosis and disruption of homeostasis. The nature of intoxication and its severity in one form or another of the disease affects the rate of breakdown of protein structures.

The conducted research substantiates the need for combination therapy in patients with CTIN, which will help eliminate the inflammatory process, excrete endotoxins from the kidney tissue, stabilize cell cytomembranes and kidney function.

For a comparative analysis of various methods of treating chronic tubulointerstitial nephritis, sick children were divided into 2 groups depending on the method of therapy. The traditional method of therapy was administered to 42 (35%) children (group 1). The main contingent of children, 30 (71.4%) were admitted to the clinic on days 3-10 from the onset of the disease, and in 12 (28.5%) cases at a later date.

Secondthe group consisted of 41 (34.1%) patients with CTIN, aged from 4 to 15 years (22 (53.7%) girls, 19 (46.3%) boys), who received the drug "Rutin" against the background of traditional therapy.

In patients with CTIN of group 2, both extrarenal and renal symptoms of the disease disappeared significantly earlier than in group 1.

The complex of therapeutic measures includes the drug “Rutin” (group 2). The choice of this drug was made taking into account its numerous positive pharmacological effects:it improves metabolic, immunological,regenerativeprocesses, has an antioxidant effect and improves the permeability of the walls of blood vessels and capillaries. One of the important advantages of the drug is its high safety.

As a result of the use of the drug "Rutin" in patients with CTIN by 11.2±0.21 (p=0.001) day we observed a transition from the active phase of the disease to the remission stage, and in the compared group clinical recovery occurred only 12.3±0.6 days from the start of treatment, which is 1.1±0.39 days later than in 2 group.

Thus, in the group of patients after treatment supplemented with the drug "Rutin" over a period of an average course of treatment of 10-11 days, the clinical signs of the inflammatory process in the urinary tract decreased and completely disappeared.

The results of studies of the EI indicator after treatment with the proposed method showed that in patients of group 2 the level of MPP in the urine had a relatively high tendency to decrease, but still remained 4 times higher than the level in healthy children and amounted to0.605±0.023 units. wholesale pl. (p1=0.001). Recovery of the studied parameter occurred on the 10-11th day of treatment. The elimination of the increased level of MPP in the urine in patients of group 1 was observed only on the 12-13th day of treatment and amounted to 1.2 ± 0.034 units. wholesale pl. (p1>0.1), which was not significant in comparison with the indicators in children of group 2.

That is, the dynamics of MPP elimination in urine occurred faster in group 2 compared to group 1, but did not reach control standards, both in dynamics and at discharge.

The use of this drug significantly increased the level of ECA, SSA and reduced the level of IT in the blood plasma, as well as MPP in the urine in children of group 2.

The increase in ECA levels in children of group 2 is likely due to the antioxidant and nephroprotective properties of the drug. We noted a more pronounced positive dynamics of the ECA indicator after the use of the drug "Rutin" in patients of group 2, which amounted to 33.04±0.5 g/l (p1=0.001) compared to group 1, where the ECA level was 30.74±0.58 g/l at discharge from the hospital (p1>0.1).

We determined that the level of SSA and IT in children of group 2 during therapy had more positive dynamics and amounted to79.4±1.2% and 0.25±0.005 arb. units

(p1=0.05 and p1=0.05), while in children of group 1 these figures were 72.2±0.6% and 0.36±0.01 conventional units. units (p1=0.05 and p1=>0.1). In healthy children, these parameters were 93±0.9% and 0.12±0.01 arb. units, respectively (Fig. 2).

Analyzing the results of the study, it was revealed that these indicators such as ECA, SSA, IT, CIA in the blood plasma, and MPP in the urine after using the drug “Rutin” had a high positive trend, but still did not reach the level in healthy children.

Apparently, “Rutin” does not have an effective enough effect on the processes of endotoxicosis that occurs in aseptic inflammatory diseases of the kidney tissue, which requires the development of new methods for its correction.

Positive dynamics were also noted when studying the functional state of the kidneys in patients of group 2.

The effectiveness of the drug "Rutin" is confirmed by a decrease in leukocyturia. Thus, leukocyturia statistically significantly decreased in patients of group 2 to 5-6 cells. in p.z. compared to group 1 (7-8 cells in the paragraph). During the therapy, more pronounced changes were noted in group 2 of children.

Analysis of the results of the study of daily proteinuria in the compared groups showed that after treatment in group 2, this indicator of urinary syndrome significantly decreased and was found only in 4 (11.4%) patients, and in children of group 1, this indicator remained elevated in 8 (25%) patients.

In the compared groups, the hematuria indicator changed in the same direction. There was a decrease in red blood cells in the urine, but in group 2 these changes were more pronounced.

After treatment, a significant increase in GFR was noted only in children of group 2 (78.0±0.9 ml/min/1.73m2 (p=0.01), while in patients of group 1 this figure was 73.8±1.56 ml /min/1.73m2(p1>0.1). The GFR indicator had significant values only in children of group 2, where it increased by 6%, and in children of group 1 only by 1%.

After treatment, GFR (measured by cystatin) increased: in patients of group 2 – from 67.4±10.3 to 83.2±9.6 ml/min/1.73 m2 (p=0.001); in children of group 1 – from 67.4±10.3 to 74.9±9.7 ml/min/1.73 m2) (p=0.02).

A predominant improvement in GFR (by cystatin) was established primarily in children of group 2 (p = 0.001); in them, the rate of increase in GFR was the highest - by 19% (in group 1 - by 10%), which is associated with the positive properties of the proposed we have a method of therapy, which is characterized by a pronounced nephroprotective, anti-inflammatory, antispasmodic, membrane-stabilizing effect of the drug “Rutin”.

When assessing the functional state of the kidneys based on the dynamics of creatinine and cystatin levels, cystatin levels are undoubtedly more reliable.UAn

increase in GFR by cystatin is observed earlier than that determined by creatinine (p = 0.02).

During treatment, an increase in daily diuresis was observed in both groups. We determined that in group 1, daily diuresis increased slightly to 4%, while in the comparison group this figure increased to 8% (p1=0.05), which corresponds to the nature of changes in FSP in TIN.

Thus, the dynamics of indicators of partial kidney functions and protein metabolism indicate that “Rutin”, having an indirect effect on the tendency towards normalization, is characterized by a significant advantage over the traditional method, to a greater extent in relation to the elimination of clinical symptoms and in terms of the level of tendency towards normalization of protein indicators metabolism in blood plasma and urine, but to a lesser extent in the dynamics of restoration of “urinary syndrome”: leukocyturia, proteinuria, hematuria and restoration of partial renal functions.

Taking into account the results of the use of the drug "Rutin" in the treatment of children with CTIN, which we obtained in previous studies (groups 1 and 2), as well as in order to optimize the positive effects and eliminate the shortcomings of treatment, we observed the 3rd group of patients who, in combination with traditional therapy, additional use of electrophoresis with 0.5% aminophylline was carried out.

Electrophoresis was performed with aminophylline 0.5% solution in warm water on the lumbar region, during sanitation of urine (on the 3-4th day of treatment), contraindication: high activity of the pathological process and impaired urodynamics.

The effectiveness of the modified method of therapy was studied in 37 sick children. Among them were 19 (51.4%) girls, 16 (48.6%) boys aged 4 to 15 years.

As a result of the use of complex therapy in patients with CTIN, on day 9.1±0.3 (p=0.001) we observed clinical recovery in all extrarenal and renal signs of the disease, and in group 2, bed days were 11.2±0. 21 days, which is significantly shorter by 2.1 days and 5 days compared to the group of children receiving traditional therapy.

Thus, complex treatment turned out to be significantly effective for all analyzed clinical symptoms of the disease compared to other groups of patients.

As a result of studying the effectiveness of complex treatment in terms of protein metabolism indicators: MPP in the urine, ECA, SSA, IT, CIA in the blood plasma in patients of group 3, we determined a significant decrease in MPP in the urine to 0.207±0.012 units. wholesale pl. (p1=0.001), regardless of the initial level of EI and the form of the disease. Whereas, in patients of group 2, the level of MPP in the urine during therapy was 0.605±0.023 units. wholesale pl. (p1=0.05).

The restoration of the studied parameter in children of group 3 occurred on days 8-9, and in the majority of patients in group 2, even on days 11-12 of treatment remained unchanged.

In addition, this modified treatment method contributed to a significant increase in the level of ECA, SSA and a decrease in IT, CIA in the blood plasma in children of group 3.

We determined that complex treatment has a positive effect on the level of ECA, which in children of group 3 was 37.5±0.3 g/l (p1=0.001, p2=0.05), while in patients of group 2, this indicator was 33.04±0.5 g/l (p1=0.05) (Fig. 3).

The dynamics of the CIA indicator in patients receiving complex modified treatment was positive in relation to that in children of group 2.

The use of complex therapy contributed to a significant increase in the level of SSA in children of group 3, which amounted to 87.9±0.3% (p1=0.001; p2=0.001), while in children of group 2 this figure was 79.4± 1.2% (p1=0.001), respectively (Table 2.).

We observed a similar picture with regard to IT, its decrease in group 3 was 44% and was significant 0.16±0.004 arb. units (p1=0.001; p2=0.05) compared to group 2, where this indicator was 0.25±0.005 conventional units. (p1=0.05) (Fig. 4).

Thus, complex treatment was combined with a statistically significant decrease in MPP in the urine, as well as an increase in ECA, SSA and a decrease in IT, CIA in the blood plasma. This effect is associated with the positive effect of complex treatment on the stability of renal cytomembranes.

Thus, analysis of the dynamics of MPP in urine, ECA, SSA, IT, CIA in the blood plasma of sick children of group 3 indicates a pronounced “antitoxic” effect of complex treatment, which makes it possible to use it to correct impaired indicators of protein metabolism in CTIN in children.

The research results indicate that complex treatment of patients in group 3 leads to a more sustainable correction of changes in partial renal functions already in the dynamics of treatment.

At the same time, the level of hematuria in children reached control values in 98%, while in children of group 2 this indicator was increased in 12% of children and amounted to 2-3 cells per cell.

The level of leukocyturia in children of group 3 after treatment became even lower than control values and amounted to 3-4 cells per cell. (p1=0.001; p2=0.001), whereas in patients of group 2 this parameter was 6-7 cells per cell. (p1=0.01), respectively, which is 2 times more than in group 3.

The level of daily proteinuria remained higher than the control value in 4 (11.4%) patients of group 2, while in patients of group 3 clinically significant proteinuria was not found in any patient, which we associate with the anti-inflammatory and reparative effect of the author’s restorative treatment regimen.

After treatment, GFR increased in both groups (respectively, 78.0±0.9 ml/min/1.73 m² and 84.75±1.72 ml/min/1.73 m². The degree of increase in GFR was: 2 group - by 7.5% and in group 3 by 15%.

GFR (based on cystatin) increased: in children of group 3 – from 67.4±10.3 to 93.8±1.61 ml/min/1.73 m2 (p=0.0003); in patients of group 2 – from 67.4±10.3 to 83.2±9.6 ml/min/1.73 m2) (p=0.02)(Fig.9.).The most positive dynamics were revealed in children of group 3 (p=0.001), twhereas this indicator in group 1 - by 7.5% and in group 2 by 17%. We associate this with the nephroprotective, anti-inflammatory, antispasmodic, reparative properties of electrophoresis with 0.5% aminophylline, which lead to improved microcirculation in the renal tissue.

When comparing GFR in children of group 3 after therapy calculated by the level of cystatin and creatinine in the blood, a higher reliability of GFR calculation by cystatin was noted (p = 0.01), which allows for a more accurate assessment of the severity and prognosis of the development of complications.

The results of the study of daily diuresis made it possible to determine that this indicator in patients of group 2 was 1.15±0.037 l/day (p1=0.05), and in group 3 it was 1.42±0.046 l/day (p1=0.05; p2=0.05), respectively, which undoubtedly indicates a “partial” advantage of the modified method of treatment.

These research results showed that the author’s method of correction of CTIN, along with a pronounced clinical effect on the elimination of extrarenal and renal pathological symptom complexes, has a positive effect not only on indicators of protein metabolism and “urinary syndrome”, but also on partial kidney functions, and contributes to their rapid reaching the level in healthy children.

In addition, the modified treatment method we propose contributes to a more sustainable correction of not only the aseptic inflammatory process, but also metabolic and partial disorders.

The positive effect of electrophoresis was due to the improvement of renal hemodynamics, tissue oxygenation, cellular metabolism, reducing the increased tone of the smooth muscles of the upper urinary tract and activating the secretory function of the kidneys; electrophoresis promotes the excretion of sand and small stones from the renal tissue into the urine. Under the influence of heat, electrical stimulation and 0.5% aminophylline, blood circulation, metabolic and reparative processes are activated, and kidney function is improved.

Conclusions: Analysis of the study results showed that the treatment method we propose is the most effective way to treat CTIN, due to the accelerated recovery of both

clinical and laboratory parameters of the disease and indicators of protein metabolism, as well as in relation to the restoration of the functional state of the kidneys, which leads to a reduction in time hospital stay, reducing the number of relapses of exacerbation, preventing complications of the chronic process.

All this helps prevent the development of disability and reduce the number of child deaths from chronic renal failure.

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