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ANALYSIS OF THE RELATIONSHIP BETWEEN VITAMIN D AND CKD

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Severe vitamin D deficiency (decreased concentration of 25 (OH) D in serum) in infants and children can cause signs of Fanconi syndrome, including phosphaturia, glucosuria, aminoaciduria and renal tubule acidosis. This indicates that vitamin D and its metabolites affect the function of the proximal tubules.

Objective: to substantiate the role of vitamin D in the progression and prognosis of CKD in children.

Results of this study demonstrate that vitamin D deficiency is common in children with CKD. Determination of vitamin D levels in children with CKD is important for timely correction and prevention of further progression of CKD. Timely replacement therapy will improve the quality of life of a child with CKD and prevent the development of complications.

Key words: children, chronic kidney disease, vitamin D deficiency, prognosis

Recently, an active search for effective and safe drugs with nephroprotective action on the one hand, and great interest in the previously unknown effects and properties of vitamin D. Administration of vitamin D to animals with uremia was accompanied by a decrease in podocyte apoptosis and loss of nephrine, a protein in the slit diaphragm, which led to a decrease in proteinuria. Vitamin D suppresses profibrotic TGF-ei, in tubular epithelial cells. Inhibition of tubulointerstitial fibrosis by vitamin D was confirmed in an animal model with unilateral ureteral obstruction. Along with the use of ACEIs and ARBs, which have been shown to be effective experimentally and clinically, we consider it advisable to investigate the use of vitamin D in the prevention and delay of nephrosclerosis progression in children with chronic kidney disease [1].

A deficiency of the active form of vitamin D calcitriol (CT) is identified in the early stages of chronic kidney disease (CKD) and progresses as the glomerular filtration rate decreases due to its reduced synthesis in the proximal tubules. Decreased CT is a consequence of CKD and at the same time accelerates its progression. In experimental studies and animal experiments, the mechanisms of action of CT have been defined: anti-inflammatory, inhibition of proliferation of mesangial cells and glomerular podocytes, reduction of renin-angiotensin system activity, prevention of glomerular hypertrophy, reduction of proteinuria, fibrogenic cytokine production, blockade of epithelial-mesenchymal transformation of tubular epithelium and activation of myofibroblasts. Through these effects CT inhibits the progression of glomerular and tubulointerstitial fibrosis and thereby slows the progression of chronic kidney disease (CKD).

However, there are as yet no prospective studies proving a renoprotective effect using reliable end results [2 -8].

CKD, and in particular terminal chronic renal failure, is associated with vitamin D deficiency and disruption of all metabolic processes associated with vitamin D. Attempts are being made to test and pharmacologically modulate its levels and thus promote greater availability of the substrate for external calcitriol production. Calcitriol production is reduced in patients with CKD not only because of a reduction in functional renal parenchyma, but also as a consequence of inhibition of 1-α-hydroxylase by FGF-23 and other factors.

On the other hand, although parathormone (PTH) increases calcitriol production by the kidneys, it also causes secondary hyperparathyroidism. Vitamin D deficiency in the general population is associated, at least in epidemiological studies, with a number of medical complications, and the same is true for patients with renal insufficiency. Although randomised trials are not available, clinical observational studies have repeatedly shown that treatment with VDR activators is associated with a better prognosis. As in other areas of medicine, nephrology is currently focusing on vitamin D and vitamin D receptor activation[3]. In 2018, the results of a study of children in the USA were published, supporting the hypothesis that vitamin D insufficiency/deficiency increases the likelihood of anaemia in children with CKD[4].

Severe vitamin D deficiency (decreased in serum 25(OH)D concentration) in infants and children can cause signs of Fanconi syndrome, including phosphaturia, glucosuria, aminoaciduria and renal tubular acidosis. This indicates that vitamin D and its metabolites affect proximal tubule function. Filtered 25(OH)D bound to vitamin D-binding protein (DBP) undergoes endocytosis by the coubilinomegalin in the apical membrane. Intracellular 25(OH)D is metabolised to 1,25(OH)2D or calcitroic acid by 1-α-hydroxylase or 24-hydroxylase in the mitochondria of tubule cells [5].

The aim was to substantiate the role of vitamin D in the progression and prognosis of CKD in children.

MATERIALS AND METHODS

Clinical observational case-control study.

The study is based at the Regional Children's Clinical Hospital, Department of Nephrology. The study will be carried out over a one-year period.

The case group includes 36 children aged 0-17 years inclusive with a diagnosis of chronic kidney disease (CKD) with vitamin D deficiency.

The control group includes 54 children aged 0-17 years, inclusive, with a diagnosis of CKD with vitamin D deficiency and with normal vitamin D levels.

The "M ± S" mean and standard deviation were used to describe the central position and the absolute dispersion of the data, while the coefficient of variation V, which characterises the homogeneity of the indicator and allows a comparison of the homogeneity of different indicators, regardless of their scale and units, was used to assess the relative dispersion. If the coefficient of variation is less than 10%, the degree of dispersion of the data is considered minor, from 10% to 20% - medium, over 20% and less or equal to 33% - significant; if the value of the coefficient of variation does not exceed 33%, the population is considered homogeneous, if over 33% - not homogeneous. To describe the structure of the indicator, median and quartiles "Me" and minimum and maximum were used to estimate the range of variation of the indicator "Min; Max".

STUDY RESULTS

1. Correlation analysis of indicators in children with CKD in the main group

Table 1. – Statistically significant correlations of laboratory and clinical parameters in children in the main group.

Characteristics	Description of criteria	Meaning of criteria	α-level	p-level
Vitamin D value, ng/ml& Stage of CKD	Spearman coefficient	0,7	0,05	P<0,05
Vitamin D value, ng/ml& SCF mL/min	Spearman coefficient	0,8	0,05	P<0,05
Vitamin D index, ng/ml& proteinuria	Spearman coefficient	-0,5	0,05	P<0,05
Vitamin D index, ng/ml& urinary c-m	Spearman coefficient	-0,4	0,05	P<0,05
Vitamin D index, ng/ml&haematuria	Spearman coefficient	-0,4	0,05	P<0,05
Vitamin D index, ng/ml& swelling	Spearman coefficient	-0,6	0,05	P<0,05
Vitamin D value, ng/ml& comorbidities	Spearman coefficient	-0,3	0,05	P<0,05
Vitamin D index, ng/ml& AG	Spearman coefficient	-0,7	0,05	P<0,05
Vitamin D index, ng/ml& sweating	Spearman coefficient	-0,8	0,05	P<0,05
Vitamin D value, ng/ml& fatigue	Spearman coefficient	-0,6	0,05	P<0,05
Vitamin D index, ng/ml& irritability	Spearman coefficient	-0,6	0,05	P<0,05
Vitamin D value, ng/ml& appetite reduction	Spearman coefficient	-0,5	0,05	P<0,05

Note: Statistical significance level p<0.05

The analysis of statistically significant correlations in children in the main group showed a strong direct relationship between vitamin D level and GFR, vitamin D level and stage of CKD. The results obtained in our study also showed a correlation between clinical signs and vitamin D level. A consistently strong inverse relationship was found between vitamin D levels and arterial hypertension, sweating, irritability, swelling, fatigue, decreased appetite.Correlation analysis showed a moderate inverse association between vitamin D levels and laboratory parameters such as proteinuria, urinary syndrome. There is also a weak inverse association between vitamin D levels and comorbidities. These factors show an association between vitamin D levels and the progression of renal disease.

2. Correlation analysis of indicators in children with CKD in the control group

Table 2 - Statistically significant correlations of laboratory and clinical parameters in children in the control group

Characteristics	Description of criteria	Meaning of criteria	α-level	p-level
Vitamin D value, ng/ml& Stage of CKD	Spearman coefficient	0,6	0,05	P<0,05
Vitamin D value, ng/ml& SCF mL/min	Spearman coefficient	0,6	0,05	P<0,05
Vitamin D index, ng/ml& proteinuria	Spearman coefficient	-0,3	0,05	P<0,05
Vitamin D index, ng/ml& urinary c-m	Spearman coefficient	-0,2	0,05	P<0,05
Vitamin D index, ng/ml&haematuria	Spearman coefficient	-0,2	0,05	P<0,05
Vitamin D index, ng/ml& swelling	Spearman coefficient	-0,5	0,05	P<0,05
Vitamin D value, ng/ml& comorbidities	Spearman coefficient	-0,3	0,05	P<0,05
Vitamin D index, ng/ml& AG	Spearman coefficient	-0,4	0,05	P<0,05
Vitamin D index, ng/ml& sweating	Spearman coefficient	-0,6	0,05	P<0,05
Vitamin D value, ng/ml& fatigue	Spearman coefficient	-0,5	0,05	P<0,05
Vitamin D index, ng/ml& irritability	Spearman coefficient	-0,5	0,05	P<0,05
Vitamin D value, ng/ml& appetite reduction	Spearman coefficient	-0,4	0,05	P<0,05

When analyzing statistically significant correlational relationships in children in the control group, a strong direct relationship between vitamin D level and GFR, vitamin D level and stage of CKD was also observed. Correlation analysis showed a moderate inverse association between vitamin D levels and clinical manifestations such as oedema, irritability, fatigue, arterial hypertension, and decreased appetite. In the control group, there is a

weak inverse association between vitamin D levels and comorbidities. There is an inverse association between vitamin D levels and laboratory parameters: haematuria, proteinuria, urinary syndrome.

In conclusion of the correlation analysis, it can be concluded that there is a strong direct correlation between vitamin D levels and GFR, vitamin D levels and chronic kidney disease, confirming the need for early diagnosis and correction of vitamin D levels and will allow early prevention of the progression of kidney disease.

CONCLUSIONS

1. In an analysis of statistically significant correlational relationships, a strong direct relationship between vitamin D level and GFR, vitamin D level and stage of CKD was observed in children in the main group. The results obtained in our study also showed the relationship between clinical signs and vitamin D level. A strong inverse relationship between vitamin D level and arterial hypertension, sweating, irritability, edema, fatigue, reduced appetite was found in a consistent manner. Correlation analysis showed a moderate inverse association between vitamin D levels and laboratory parameters such as proteinuria, urinary syndrome. There was alsoa weak inverse association between vitamin D levels and comorbidities.

2. In children in the control group, there was also a strong direct association between vitamin D levels and GFR, vitamin D levels and the stage of CKD. Correlation analysis showed a moderate inverse association between vitamin D levels and clinical manifestations such as oedema, irritability, fatigue, hypertension and reduced appetite. In the control group, there is a weak inverse association between vitamin D levels and comorbidities. There is an inverse association between vitamin D levels and laboratory parameters: haematuria, proteinuria, urinary syndrome.

3. The results of this study show that vitamin D deficiency is common in children with CKD. Determination of vitamin D levels in children with CKD is important for the timely correction and prevention of further progression of CKD. Timely initiation of replacement therapy will improve the quality of life of the child with CKD and prevent the development of complications.

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D ВИТАМИНІ МЕН БСА АРАСЫНДАҒЫ БАЙЛАНЫСТЫ ТАЛДАУ

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Мақалада D дәрумені мен оның метаболиттері проксимальды түтікшелердің жұмысына әсер ететіндігі көрсетілген.

Мақсат. балалардағы БСА прогрессиясы мен болжауындағы D витаминінің рөлін негіздеу.

Бұл зерттеудің нәтижелері БСА бар балаларда D витаминінің жетіспеушілігі жиі кездесетінін көрсетеді, БСА бар балаларда D витаминінің деңгейін анықтау БСА одан әрі дамуын уақтылы түзету және алдын алу үшін маңызды. Уақытында басталған алмастыру терапиясы БСА бар баланың өмір сүру сапасын жақсартады және асқынулардың дамуына жол бермейді.

Кілт сөздер: балалар, бүйректің созылмалы ауруы, D витаминінің жетіспеушілігі, болжау

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АНАЛИЗ СВЯЗИ МЕЖДУ ВИТАМИНОМ D И ХБП

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Статья указывает на то, что витамин D и его метаболиты влияют на функцию проксимальных канальцев.

Цель – обосновать роль витамина D в прогрессировании и прогнозировании ХБП у детей.

Результаты данного исследования демонстрируют, что у детей с ХБП распространен дефицит витамина D. Определение уровня витамина D у детей с ХБП является важным для своевременной коррекции и предотвращения дальнейшего прогрессирования ХБП. Вовремя начатая заместительная терапия улучшит качество жизни ребенка с ХБП и предупредит развитие осложнений.

Ключевые слова: дети, хроническая болезнь почек, дефицит витамина Д, прогнозирование