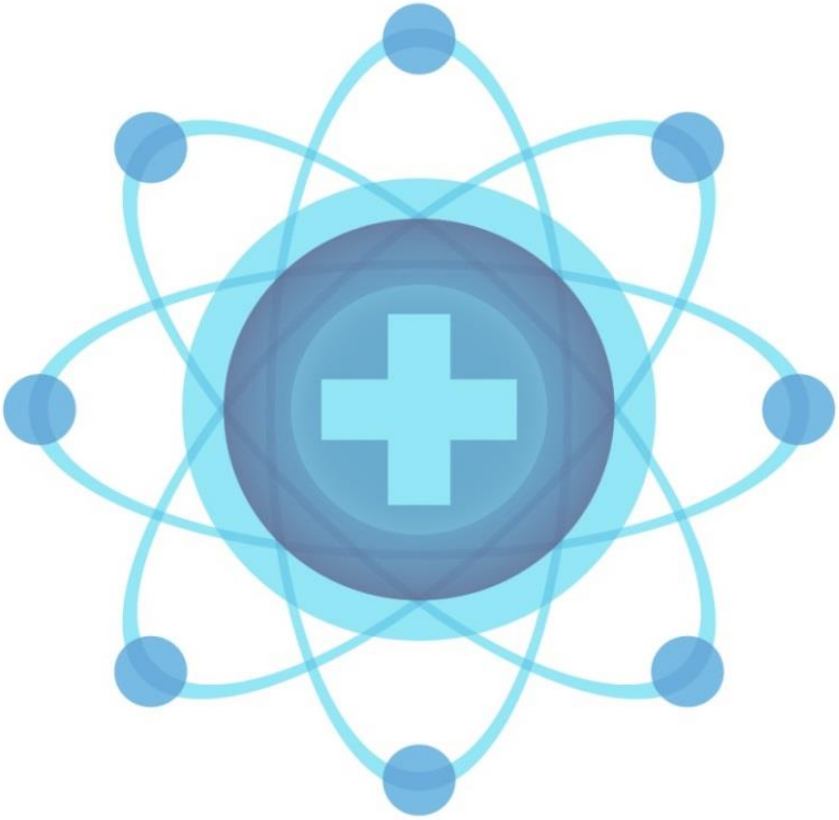

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A NEW LOOK FOR THE TREATMENT OF RESTLE LEG SYNDROME

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Abstract. The article presents the results of treatment of patients with primary restless legs syndrome (RLS). The patients were divided into two groups: with and without the inclusion of vitamin D (colcalciferol) in the treatment regimen. The results of therapy showed a more pronounced positive effect in patients who received vitamin D in complex therapy, which manifested itself in a more pronounced improvement in the clinical picture, a decrease in the severity of RLS, an improvement in sleep and the psycho-emotional state of patients.

Keywords: restless leg syndrome, vitamin D, drowsiness

Restless legs syndrome (RLS) or Willis-Ekbom syndrome is an obsessive chronic condition that significantly reduces the quality of life of patients due to developing insomnia, depression and other somatic and psychological complications. The syndrome is characterized by discomfort mainly in the legs, less often in the arms, they appear at rest, forcing the patient to make movements to alleviate the symptoms.

Restless legs syndrome seriously affects the quality of life and disrupts sleep, which indicates the need for medical treatment. Many countries around the world recommend starting RLS therapy with dopamine receptor agonists (pramipexole, ropinirole, or rotigotine transdermal patch). These drugs are approved in most countries of the world. In addition, α-2-δ ligands are recommended (gabapentin enacarbil approved in the US and Japan). In Europe, opioids (long-acting oxycodone-naloxone) are also approved as second-line therapy for severe RLS. Iron supplements are effective in secondary RLS, while benzodiazepines and other anticonvulsants are not recommended or supported by many scientific studies. There is much less evidence for the effective treatment of RLS associated with other conditions such as uremia or pregnancy. In addition, there are very few data on the management of RLS when first-line treatment fails or when patients develop augmentation.

In our study, laboratory studies revealed a significant decrease in vitamin D in the blood and a decrease in the index of nerve growth factor that correlates with this.

In the context of the data obtained, we set ourselves the goal of determining the effectiveness of complex therapy for RLS, its effect on the severity and level of drowsiness, depression and quality of life.

Material and methods of research: Patients with primary RLS (n=28) are subdivided into:

Subgroup 1 - 10 patients who received basic therapy, including pramipexole (taken in the evening 2 hours before bedtime, at a dosage of 0.125-0.25 mg;

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Subgroup 2 - 18 patients who received against the background of basic therapy including pramipexole (the reception was carried out in the evening 2 hours before a night's sleep, at a dosage of 0.125-0.25 mg and vitamin D (colcalciferol 7000 IU. Patients of the two subgroups were comparable in terms of sex, age, disease duration, 25(OH)D level, nerve growth factor, disease severity, and psychoemotional changes. Basic therapy in the study groups included vascular, metabolic, vitamin therapy, as well as a dopamine receptor agonist (pramipexole).

Vitamin D was prescribed in a daily dosage of 7000 IU (according to the criteria of the International Society of Endocrinologists), the duration of its administration varied from the level of 25 (OH) D), in the presence of concomitant hypocalcemia, calcium preparations were prescribed, if necessary, magnesium preparations (if there were complaints of cramps and determination in magnesium levels in the blood). Colecalciferol (coledan) was prescribed as a vitamin D preparation. The effectiveness of therapy was evaluated after 8 and 16 weeks.

For a comparative analysis of the effectiveness of complex therapy for RLS, an analysis was made of the effect of this therapy on the subjective and objective symptoms of the disease using a number of scales for assessing the severity of RLS. The effectiveness of therapy was assessed by changes in the scale indicators: according to the scale for assessing the severity of RLS of the International Restless Legs Syndrome Study Group (The International Restless Legs Syndrome Study Group, 2003); the level of daytime sleepiness was assessed using the Epworth Sleepiness Scale; the degree of depression was assessed using the CES-D scale. Quality of life indicators were studied using: RLS Quality of Life (RLS-QoL) Scale

Results of the study: The results of the study showed the effectiveness of basic therapy, including a dopamine receptor agonist, in leveling the main clinical signs of RLS (sensory disturbances in the limbs, involuntary movements of the limbs during sleep, sleep disturbance, daily activity). There was a decrease in the severity of RLS according to the International Restless Legs Syndrome Study Group scale and the level of insomnia in both groups. However, higher efficiency was noted in the group with the inclusion of vitamin D in the treatment regimen.

Table 1 shows the results of a comparative analysis of the results of therapy in the group with primary RLS. As can be seen from the table, in both subgroups there is a positive trend in most indicators (severity, level of insomnia, quality of life), however, significant differences were found in the group with the inclusion of vitamin D in the treatment regimen. group significantly more often go to milder severity (2 patients from severe to moderate and 7 patients from moderate to mild and in 2 patients (11%) by the end of 16 weeks there were no symptoms of RLS. This positive trend correlated with a decrease in the degree of depression, assessed on the CES-D scale. In both subgroups, there is a decrease in the severity of depression (the proportion of patients with severe depression in both subgroups decreased - twice in the first and 3 times in the second subgroup, respectively, the proportion of patients with moderate depression slightly increased (30% and 34%, respectively) and with mild depression (30% and 22%, respectively). severe RLS 2 subgroups in 4 (22%) patients there were no signs of depression by the end of therapy ($P<0.05$)

Table 1.

Comparative dynamics of subjective symptoms in the group with primary RLS against the background of basic therapy and therapy with the inclusion of vitamin D

-	1st subgroup, n=10 Basic therapy				2nd subgroup, n=18 Basic therapy + vitamin D			
	before treatment		after treatment		before treatment		after treatment	
	Abs.	%	Abs.	%	Abs.	%	Abs	%
RLS severity scale Very heavy	-	-	-	-	-	-	-	-
heavy	5	50%	3	30 %	6	33,3 %	4	**22 %**
Moderate	3	30%	2	20 %	8	44,4 %	3	17%
light	2	20%	5	50 %	4	22,2 %	9	**50 %**
No symptoms	-				-		2	**11 %**
CES-D Very severe depression	-	-	-	-	1	5,5 %	-	-
severe depression	6	60	3	**30**	11	61%	4	**22 %**
moderate depression	2	20	2	20	4	22%	6	**34 %**
mild depression	2	20	3	30	3	16%	4	22%
No depression	1	10	2	20	-	-	4	**22 %**
RLS QoL	55,5±4,5 points		65,4±5,2 points		50,1±2,4 points		**77,5±3,2** points	
Epworth scale Severe drowsiness	3	30%	2	20 %	6	33,3 %	2	**11,1 %**
Moderate sleepiness	6	60%	6	60 %	10	55,5 %	8	44,4 %
No sleepiness	1	10%	2	20 %	2	11,1 %	8	**44,4 %**
25 (OH)D (ng/ml)	15,57±1,153		14,8±1,5		13,02±1,132		**29,5±2,5**	
FRN	1045±26,2		1123±35,2		1042±24,1		**1356,44± 38,93**	

Significantly differences with data before treatment **are highlighted in bold.**

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The positive dynamics of the clinical picture was accompanied by an increase in the concentration of vitamin D and nerve growth factor only in the second subgroup (the correlation coefficient of the concentration of 25(OH)D and NGF had a negative and significant relationship with the clinical manifestations of RLS). In subgroup 2, which received complex therapy with vitamin D, the concentration of 25(OH)D increased from 13.02±1.13 to 29.5±2.5 ($p<0.001$) at the 16th week. An increase in the concentration of vitamin D was accompanied by a significant increase in the concentration of NGF (from 1042±24.1 to 1356.44±38.93, ($p<0.01$)), while in 1 subgroup that did not receive vitamin D, a natural increase in the concentration of vitamin D was not observed. . This was accompanied by an insignificant increase in the concentration of NGF (from 1045±26.2 to 1123±35.2, ($p<0.1$)).

The results of the treatment showed the effectiveness of the complex therapy of patients with RLS, with the inclusion of the dopamine receptor agonist pramipexole and vitamin D in the complex therapy. Pramipexole was prescribed 0.25 mg ½ tab. IU (colcalciferol). Positive dynamics was manifested in a decrease in the severity of RLS symptoms, a decrease in the degree of daytime sleepiness and the level of depression, which was accompanied by an increase in the quality of life according to the RLS QoL scale. This complex of therapy led to an increase in the concentration of vitamin D in the blood serum, which had a positive effect on the level of nerve growth factor. The results obtained confirm the neurosteroid properties of vitamin D, in particular, in the regulation of the activity of the nervous system, which is manifested by an increase in neurotrophic factors.

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