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NEW ASPECTS OF TREATMENT OF COMPLICATIONS OF MENINGOENCEPHALITIS IN CHILDREN

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Abstract:

Favourably ended meningoencephalitis in childhood, can in the remote period manifest itself by neurological deficit in the form of mnemastic and sensory insufficiency. Transition from acute to chronic neuroinfection depends on the disturbances in the limbic area of the brain, and the timely use of etiotropic treatment obtained early will prevent severe complications. Such a drug is cerebralizine, and the improved method in the form of ozonation of cerebralizine will enhance its action and reduce the rehabilitation period(1,10).

Keywords: Children, Sequelae Of Meningoencephalitis, FIM Scale, Neuroimaging, Ozonized Cerebrolysin

INTRODUCTION:

Even benignly ended meningoencephalitis (MEF) can later end in a neurological defect in the form of limitation of the mnemastic and sensory sphere in children. It is the transition of acute neuroinfection to a chronic state that is a factor in the development of abnormal functioning of the limbic area of the brain (4, 6, 9). The course and outcome of the disease, influenced by the timely use of etiotropic treatment, but there is no guarantee of complete recovery of the patient, which is probably due to the influence of highly virulent, mutant and resistant strains of the virus on the process of nervous system disorders (1, 3, 7). In 2005, Veinberga, drew attention to the drug cerebralysin, which in his opinion prevents toxicity of stimulating neurons, improves neuroimmune and neurotransmitter indicators, as well as stabilizes the neurophysiological parameters (2, 5, 8,12). In world therapeutic practice the ways to improve efficiency of the used drugs are widely used, one of such methods of therapy is ozonation of drugs, first of all, as a safe method, secondly, interaction with ozone, drugs decrease in toxicity, increasing their own efficiency, improves blood transport function and oxygen supply of ischemic tissues, restores energy formation in cells (10, 11). Thus, the relevance of the work lies in the improvement of the method of treatment of encephalitis in the remote period.

OBJECTIVE: To evaluate the effectiveness of treatment of meningoencephalitis sequel in children with ozonized cerebralysin.

MATERIAL AND METHODS OF RESEARCH. The study is based on clinical and neurological examination of children with consequences of meningoencephalitis (MEF) of 56 children, including 12 girls, 44 boys. The work was performed on the basis of 1 Samarkand State Medical University clinic in the department of pediatric neurology for the period 2015-2021. The diagnosis of meningoencephalitis was established based on generally accepted criteria according to ICD-10 classification (WHO, 1992). The degree of neurological deficit was assessed using the FIM (Functional Independence Measure (1979)) scale, and this scale was used to evaluate the effectiveness of rehabilitation treatment. The total score on the FIM scale ranged from 18 to 126 points, the lower the level, the greater the degree of dependence on others in daily life, the normal score corresponded to - 110-126 points. In addition to the standard clinical and neurological examination, with a thorough anamnesis beforehand, patients underwent neuroimaging (MRI studies), PEG electroencephalography if necessary. Patients were divided into groups: Group I received traditional therapy and consisted of 31 children, Group II received treatment with ozonized cerebralysin (OC) and consisted of 25 children. Patients received OC for 5-6 courses, each course of 10 OC intakes. In addition, the patients were divided into subgroups depending on the duration of the disease (I subgroup of 4-6 years, and II subgroup of more than 6 years).

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Study Results: Clinical signs in children with pMEF are presented in Table 1.

Table 1.

Comparative analysis by FIM1 scale subgroup in group I and group II patients with MEF sequelae

Motor functions	Before treatment		After treatment	
	Group I (n=14)	Group II (n=12)	Group I (n=14)	Group II (n=12)
	Score		Score	
1. Food intake (using cutlery, bringing food to the mouth, swallowing)	3,4±0,29	2,9±0,23	3,5±0,25	6,3±0,13
Personal hygiene (brushing teeth, combing hair, washing face and hands)	2,1±0,38	2,2±0,17	2,6±0,27	6,1±0,19
3. Bathing/showering (washing and wiping the body, except for the back area)	2,1±0,30	1,8±0,18	2,6±0,27	6,0±0,21
Dressing (including putting on prostheses/orthotics), upper body (above waist)	2,1±0,33	2,3±0,18	2,6±0,27	6,2±0,24
5. Dressing (including putting on prostheses/orthotics), lower torso (below waist)	2,3±0,40	2,2±0,17	2,8±0,33	6,2±0,24
6. Toilet (using toilet paper after going to the toilet, hygiene bags)	2,1±0,37	1,9±0,19	2,6±0,33	5,9±0,23
Average score	2,4±0,21	2,2±0,16	2,8±0,15	6,1±0,06
Control of pelvic organ function	Before treatment		After treatment	
	Group I (n=14)	Group II (n=12)	Group I (n=14)	Group II (n=12)
	Score		Score	
7. Bladder (control of urination and, if necessary, use of urinary devices - catheter, etc.)	3,7±0,37	3,0±0,23	3,9±0,35	6,1±0,19
8. Rectum (control of defecation and if necessary, use of special equipment - enema, colostomy bag, etc.)	3,6±0,39	3,1±0,23	3,7±0,37	5,8±0,21
Average score	3,7±0,05	3,1±0,05	3,8±0,10	6,0±0,15
Moving	Before treatment		After treatment	
	Group I (n=14)	Group II (n=12)	Group I (n=14)	Group II (n=12)
	Score		Score	
9. Bed, chair, wheelchair (ability to get out of bed and lie down on bed, sit on chair or wheelchair and get up from them)	2,7±0,41	2,5±0,23	3,2±0,33	5,5±0,15
10. Toilet (ability to use toilet - sit and get up)	2,2±0,39	2,3±0,22	2,6±0,34	5,3±0,14

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11. Bathtub, shower (ability to use shower stall or tub)	1,8±0,32	1,7±0,19	2,3±0,29	5,3±0,13
12. walking/moving with a wheelchair (the ability to walk for 50 meters without assistance corresponds to the score of 7, and the inability to walk for more than 17 meters to the score of 1)	2,6±0,34	2,3±0,28	2,8±0,30	5,4±0,15
13. Climbing stairs (for 7 points, climbing 12 to 14 stairs without assistance, and for 1 point, climbing more than 4 stairs is impossible).	1,6±0,25	1,8±0,22	2,0±0,21	4,9±0,15
Average score	2,2±0,22	2,1±0,16	2,6±0,21	5,3±0,10
INTELLECT	Before treatment		After treatment	
	Group I (n=14)	Group II (n=12)	Group I (n=14)	Group II (n=12)
	Score		Score	
14. Perception of external information (speech and/or writing comprehension)	2,7±0,32	2,3±0,13	2,8±0,30	4,8±0,11
15. Expressing one's own desires and thoughts (verbally or in writing)	1,5±0,25	1,8±0,18	1,9±0,23	4,9±0,08
16. Social integration (interactions with family members, caregivers, and others in the community)	1,9±0,30	2,2±0,17	2,3±0,24	4,9±0,15
17. Decision-making (the ability to solve problems related to financial, social and personal needs).	1,4±0,20	1,5±0,15	1,8±0,19	3,9±0,08
18. Memory (ability to remember and recall visual and auditory information, learn, recognize others)	2,6±0,27	2,4±0,19	2,6±0,27	5,5±0,26
Average score	2,0±0,27	2,0±0,17	2,3±0,19	4,8±0,26

When interpreting the results obtained in children of the 1st subgroup (duration of illness from 4 to 6 years), independent eating without parental assistance, bringing food to the mouth and swallowing in children in the 1st group was before treatment in 4 patients (2,90,21 points), after treatment this index increased in 5 patients and on the scale was 3,50,21 points. In the second group this index after using OC with traditional treatment showed the following results: 7 patients had independent food intake. According to the scale, it was 4,60,10 points.

In brushing teeth, brushing hair, washing face and hands, using toilet paper in group 1 patients after treatment insignificant progress was obtained. In 3 patients there was a performance of the above mentioned skills, in comparison with Group 2 children there was a positive progress and the scale was 4,60,10 points.

Evaluating the motor functions in the second subgroup, the average score of the above mentioned parameters was: in group I before treatment 2,60,06 after treatment 3,20,10 points, in group II before treatment 3,00,14, after treatment 4,60,10 points.

In the 1st subgroup, 2 (18.2%) patients with pMEF in group I and 4 (50%) patients in group II had hemiparesis and tetraparesis. In group I, 4 (36.4%) and in group II, 3 (37.5%) patients had hemiparesis, respectively. After treatment, hemiparesis persisted in group I, and mild active movements appeared in one patient with tetraparesis. In group II, in 2 (25%) patients hemiparesis passed to a mild degree and the patients could walk independently without assistance, according to the scale it was 4.90.23 points. Of the 3, 1 (12.5%) patient with tetraparesis had decreased muscle tone as he too began to walk with the help of a stick or bystanders. The movement scale was

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estimated as follows: in group I after treatment 3.4±0.12 points and in group II 4.3±0.18 points. Patients after treatment with the traditional method showed a 6.8% improvement, and in Group II, a 12.2% improvement. Cognitive development was delayed in 10 (52,6%) patients (6 (54,5%) in Group I and 4 (50%) in Group II). After traditional treatment, 5 patients had impaired attention to speech comprehension. Patients' intelligence improved significantly better with DC with traditional treatment than with traditional treatment. Speech comprehension improved in 25% of patients, and verbal base increased. The condition improved from severe to moderate severity and was scored on a scale of 2.80.19.

Table 2.
Comparative analysis by FIM2 scale subgroup in group I and II patients with MEF squealed

Motor functions	Before treatment		After treatment	
	Group I (n=11)	Group II (n=8)	Group I (n=11)	Group II (n=8)
	Score		Score	
1. Food intake (using cutlery, bringing food to the mouth, swallowing)	2,9±0,21	3,5±0,38	3,5±0,21	5,0±0,19
Personal hygiene (brushing teeth, combing hair, washing face and hands)	2,5±0,21	2,8±0,25	3,2±0,33	4,4±0,26
3. Bathing/showering (washing and wiping the body, except for the back area)	2,5±0,16	2,9±0,30	3,1±0,16	4,6±0,18
Dressing (including putting on prostheses/orthotics), upper body (above waist)	2,6±0,20	3,4±0,42	2,8±0,23	4,8±0,16
5. Dressing (including putting on prostheses/orthotics), lower torso (below waist)	2,6±0,20	2,6±0,42	3,3±0,24	4,4±0,18
6. Toilet (using toilet paper after going to the toilet, hygiene bags)	2,5±0,16	2,9±0,40	3,1±0,16	4,4±0,32
Average score	2,6±0,06	3,0±0,14	3,2±0,10	4,6±0,10
Control of pelvic organ function	Before treatment		After treatment	
	Group I (n=11)	Group II (n=8)	Group I (n=11)	Group II (n=8)
	Score		Score	
7. Bladder (control of urination and, if necessary, use of urinary devices - catheter, etc.)	3,2±0,26	3,8±0,37	3,7±0,19	4,6±0,18
8. Rectum (control of the act of defecation and if necessary the use of special devices - enema, colostomy bag, etc.)	3,0±0,30	4,0±0,46	3,6±0,20	4,8±0,25
Average score	3,1±0,10	3,9±0,10	3,7±0,05	4,7±0,10
Moving	Before treatment		After treatment	

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	Group I (n=11)	Group II (n=8)	Group I (n=11)	Group II (n=8)
	Score		Score	
9. Bed, chair, wheelchair (ability to get out of bed and lie down on bed, sit in and out of chair or wheelchair)	3,0±0,27	3,0±0,53	3,7±0,27	4,4±0,18
10. Toilet (ability to use toilet - sit and get up)	2,7±0,19	2,4±0,38	3,5±0,28	4,0±0,19
11. Bathtub, shower (ability to use shower stall or tub)	2,4±0,15	2,5±0,33	3,3±0,19	4,1±0,13
12. walking/moving with a wheelchair (the ability to walk for 50 meters without assistance corresponds to the score of 7, and the inability to walk for more than 17 meters to the score of 1)	2,9±0,16	3,5±0,53	3,5±0,21	4,9±0,23
13. Climbing stairs (point 7 means you can climb 12-14 stairs without assistance, point 1 means you cannot climb more than 4 stairs)	2,1±0,28	2,1±0,40	3,0±0,33	3,9±0,23
Average score	2,6±0,17	2,7±0,25	3,4±0,12	4,3±0,18
INTELLECT	Before treatment		After treatment	
	Group I (n=11)	Group II (n=8)	Group I (n=11)	Group II (n=8)
	Score		Score	
14. Perception of external information (speech and/or writing comprehension)	1,9±0,21	2,3±0,45	2,5±0,16	3,3±0,31
15. Expressing one's own desires and thoughts (verbal or written)	1,4±0,15	1,5±0,38	2,2±0,23	3,1±0,13
16. Social integration (interactions with family members, caregivers, and others in the community)	1,8±0,23	2,0±0,38	2,5±0,21	2,9±0,30
17. Decision-making (the ability to solve problems related to financial, social and personal needs).	1,5±0,16	1,6±0,32	2,4±0,24	2,4±0,26
18. Memory (ability to remember and recall visual and auditory information, learn, recognize others)	1,5±0,16	1,6±0,38	1,9±0,09	2,3±0,25
Average score	1,6±0,10	1,8±0,15	2,3±0,11	2,8±0,19

The diagram shows that in the 2nd subgroup the changes after treatment are not satisfactory enough. This is due to

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the complete death of neurons in the lesion focus, which dictates the need to start therapy in the earliest possible time. The score in Group I did not differ much from that in Group II of the study patients. The score was 3,20,09 points before treatment in group I and 3,50,07 points after treatment in group II and 3,60,03 points before treatment and 3,80,08 points after treatment, respectively.

Analysis of motor function neurological status in the group of patients who received traditional treatment showed different dynamics in Group I patients. Relatively better scores were obtained in the group of patients who received traditional therapy with intravenous administration of OC. Having initially equal scores for motor function, Group II already showed better eating, personal hygiene and dressing (4.9 and 5.0 scores respectively) two months after treatment. In Group I, these values were much lower and amounted to 4.4 points on the FIM scale at month 3-4, which was (by 1.5 points) lower than in Group II. At month 3, the motor function score was 4.90.02 in group II, respectively, while in group I patients corresponded to 2.80.16 points. As can be seen in the diagram, the use of OCs improved hand muscle function and strength in group II patients with pMEF from 3.6±0.07 points to 3.8±0.09 points.

In pMEF over 6 years, there were 9 (81.8%) patients in the 2nd developmental subgroup (5(8.3%) in group I, and 4(80%) in group II). After traditional treatment with OC, 6 patients' impaired attention to speech comprehension, improved ability to play with toys, and fetching their own things persisted. Only one (16.7%) added a few words in speech, with a FIM score of 2.90,23. The patients' intelligence did not improve with traditional treatment, with a FIM score of 2.80.07 on the FIM scale. And in the group of children who had undergone MEF for 4 to 6 years, before post-treatment α-rhythm scores decreased slightly, as well as the progress of alpha rhythm modulation in the first and second groups. When evaluating β, τ, and δ rhythms, the frequency decreased and the modulation of rhythms improved insignificantly.

Table 3.
EEG1 subgroup index in group I and II patients with consequences of MEF

№	Rhythms	Before treatment		After treatment	
		I group	**II** group	I group	**II** group
		Frequency	Frequency	Frequency	Frequency
1	α-rhythm	45,2±0,94	52,3±1,17	32,8±0,95*	29,3±1,1**
2	β-rhythm	12,4±1,23	10,8±0,94	8,9±1,2**	6,1±0,91**
3	τ-rhythm	110,7±1,06	102,7±1,42	80,4±1,08*	59,1±1,11**
4	δ-rhythm	106,2±1,32	105,9±1,69	78,4±1,3*	60,2±1,34*
5	Peak wave	109,3±0,74	99±0,38	78,3±1,03**	72,2±2,25**

*Note: reliability of the results in relation to the initial condition -*P<0.05, -**P<0.001*

In the group of children with MEF more than 6 years old, before and after treatment, the indices of functional activity of the cerebral cortex improved insignificantly, as shown in the table below.

Table 4.
EEG2 subgroup index in group I and II patients with consequences of MEF

№	Rhythms	Before treatment		After treatment	
		I group	II group	I group	II group
		Frequency	Frequency	Frequency	Frequency
1	α-rhythm	50,8±1,39	59,4±0,77	43±1,35*	44,5±0,69**
2	β-rhythm	12,1±1,87	10,6±1,25	10,2±1,63*	8,3±1,66**
3	τ-rhythm	107,8±1,06	106±1,69	87±1,16**	81,2±1,56**
4	δ-rhythm	107,7±1,95	109±1,83	88,7±2,13*	85,2±1,96*
5	Peak wave	98,8±0,86	108,2±1,78	80,9±0,84*	83±1,48*

*Note: reliability of the results in relation to the initial condition -*P<0.05, -**P<0.001*

Thus, children who have undergone MEF show diffuse disturbances on the EEG, as, there are generalized changes in the cortex or subcortical structures. Minor changes in the β-rhythm were manifested by polymorphic waves. Frequently detected peak waves during EEG recording revealed foci of epileptic activity and periodic flashes of bilateral-synchronous pathological oscillations, indicating the involvement of brain stem regions in the process. With the development of limited MEF changes, persistent local pathological foci appear, which may be important in the prognosis of the subsequent course in the remote period. After our treatment, the EEG changes were characterized by residual manifestations, corresponding to the degree of residual changes in the

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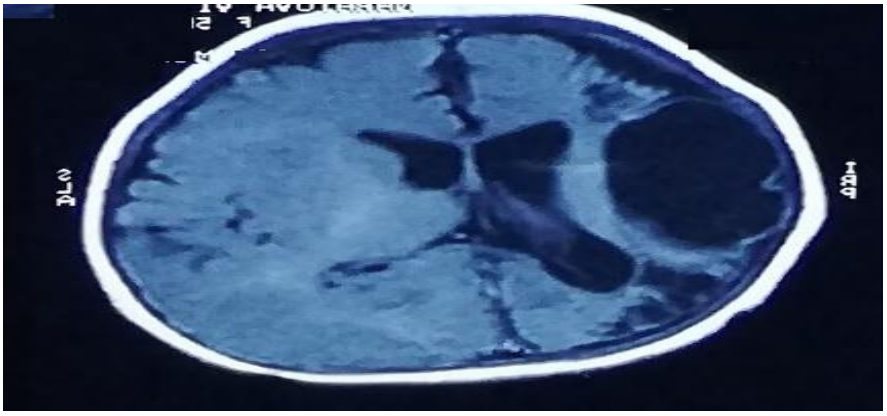
brain. Epileptic discharges were often observed, which may have an unfavorable prognostic value.

According to neuroimaging data, in children with the disease duration up to six years, brain structure atrophy was more concentrated in the cerebellar region, in 2 (25%) patients. After conventional treatment with OC, the atrophic process in the cerebellum remained.



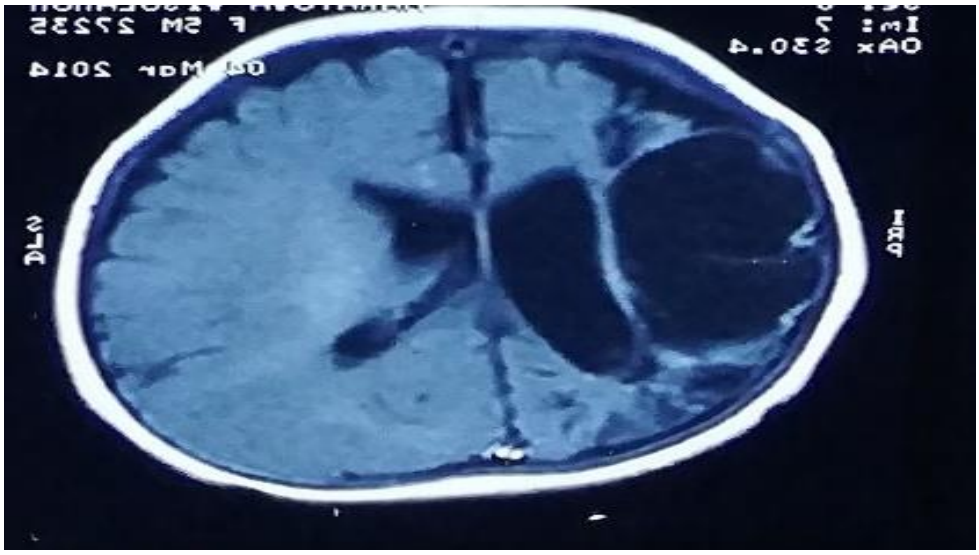


Fig. 1. MRI picture, T1 mode. Porencephalic cyst in a large size
Fig. 2. MRI picture, T1 mode, after treatment the poroencephalic cyst was sized

Comparative results of the conducted treatment both traditional and traditional with OC in the group of children with the disease duration more than six years appeared to be ineffective, confirmation of this is practically unchanged clinical and neurological symptoms and neuroimaging parameters, in 66,7% with lpMEF2, signs of cerebral atrophy were noted (on the background of treatment), the main criteria of which are: relative enlargement of arachnoidal slits, relative ventriculomegaly, indistinct demarcation between gray and white matter, accentuation of furrows and gyrations.

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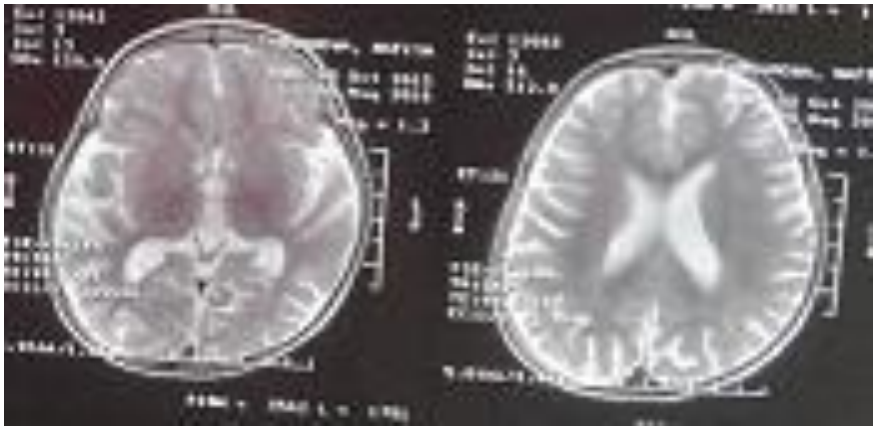

Figure 3. Enlargement of arachnoidal slits, relative ventriculomegaly, indistinct demarcation between gray and white matter, and accentuation of furrows and convolutions

Thus, the results of analyses before and after treatment of children with meningoencephalitis sequelae, according to neuroimaging images, showed characteristic changes depending on the duration of the disease, age, timing of initial treatment and specific features of additional therapy, in particular the introduction of ozonated cerebrolysin. Thus, if the use of traditional therapy in the remote period forms pathological foci with porencephalic cysts, cortical atrophy with calcifications in the projections of subcortical nuclei, hydrocephalic increases, with microcirculatory disorders and a tendency to progression. Tho, in cases of using traditional treatment with ozonated cerebrolysin in the same terms, a clear picture of the effectiveness of the absence of inflammatory swelling on the part of the brain substance, restoration of inactive neurons around the inflammatory focus of the brain, diffuse cortical atrophy persists in a small percentage, as well as hydrocephalus, with the predisposition of complete recovery of pathological lobular processes.

The study of brain metabolism using PET with 18F-FDG after treatment of 2 patients revealed a decrease in the number of foci of hypometabolism in the frontal region of the brain.

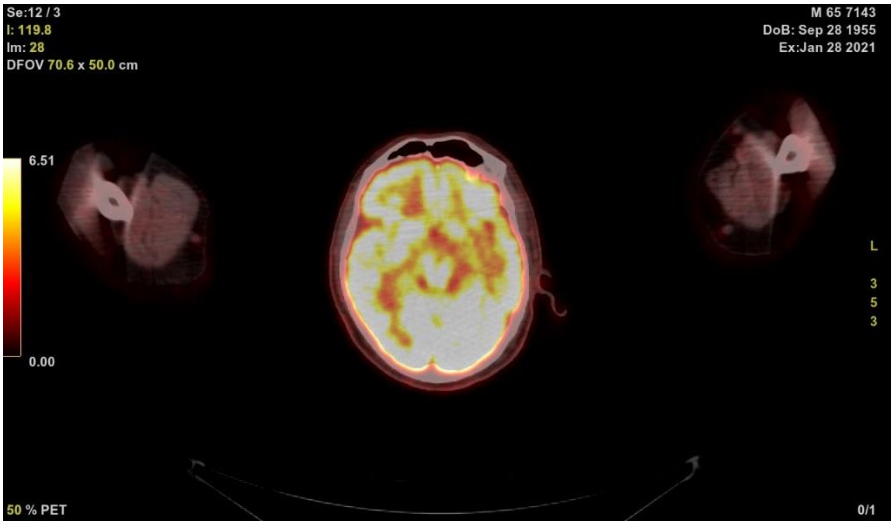

Figure 4. PET in a patient with a history of MEF of 6 years. There is hypometabolism of the frontal lobes compared to the rest of the brain

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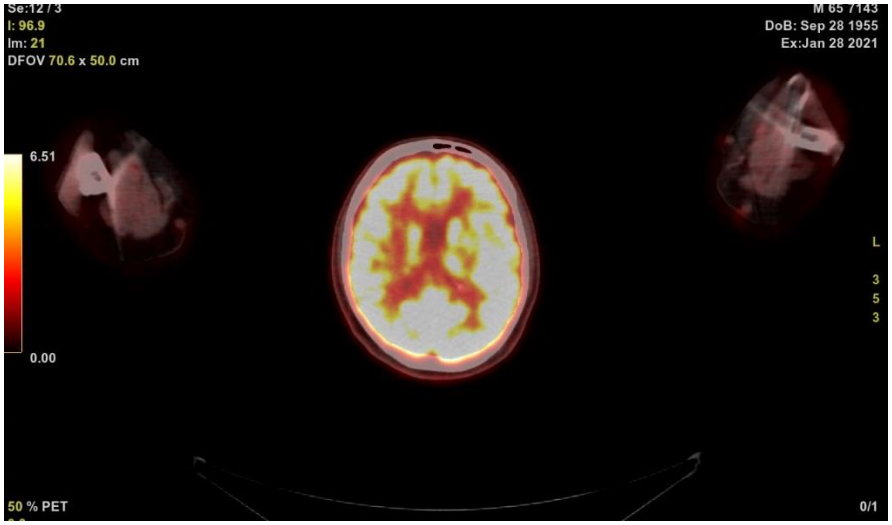

Fig. 5. PET in a patient with a history of MEF of 4 years. PET shows asymmetrical density reduction in both the lateral and mesial parts of the temporal lobe

CONCLUSIONS: Thus, the use of PET with 18F-FDG to monitor neuroprotective therapy in pMEF allowed to establish a reliable improvement in the level of functional activity of the large hemispheres, (in contrast to MRI) revealed a tendency to reduce the number of hypometabolism foci. The obtained PET data allow us to conclude about the positive effect of the conducted treatment with ozonated cerebrolysin.

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