EMBRYONIC STEM CELLS IN AMYOTROPHIC LATERAL SCLEROSIS

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Depth, quality and specificity of Cell Therapy effects in many conditions and diseases are far beyond the capacity of any other modern method

CELL THERAPY is administration of embryonic cell suspensions containing stem cells that

- remain to live there:
- allocate in tissues and organs;
- produce generations of new cells;
- restore functional activity of tissues and

Indications for treatment

- Progressive course of the disease (decrease of Karnofsky Index by more than 20% within last 6 months).
- Ineffectiveness of routine treatment. After 2000:
- Confirmed ALS.

Contraindications in ALS

- 1. Respiratory manifestations stage III respiratory insufficiency.
- 2. Inability to swallow, G-tube.
- 3. Duration exceeding 3 years.

Embryonic stem cells are capable of migration, establishment of intercellular links, proliferation, differentiation, and response to effects.

They can produce considerable amounts of biologically active substances, e.g. hematopoietic growth factors, interleukins, nerve growth factor, tumor necrosis factor, angiogenic and neutrophilic factors etc.

ESC-related Contraindications

(ESC transplantation is possible after active treatment

2. Acute thromboses (treatment is possible not earlier than

3. Acute hemophtalm (treatment is possible after 3 months).

culitis, thromboses, pneumonia, development of acute

4. Expressed pulmonary hypertension secondaray to vas-

6. Terminal stage of the disease (expressed intoxication,

7. Chronic infection lesions (preliminary treatment is

advanced metabolic dysfunctions and decompensation

1. Exacerbated vasculitis: capillaritis, phlebitis, arteritis

resulting in remission, after 3 months).

after 3-6 months).

of internal organs).

required).

or subacute pulmonary heart.

5. Myelocarcinosis, myelofibrosis.

Embryonic stem cells are characterized by weaker immune response than mature cells due to late expression of histocompatibility antigens in the process of maturation

Embryonic stem cells contain much lower counts of highly effective cells such as leukocytes, endothelium of vessels, dendrite cells etc.

During the embryonic period, transplants do not have mature lymphocytes, and are tolerated by recipients

At present, applied are suspensions prepared from embryonic brain, bone marrow, liver, spleen, thymus, pancreas, and culocutaneous graft.

Diagnosis was confirmed by neurologists from different countries - USA, Germany, Italy, Greece, India, Russia, Ukraine, Sweden on the basis of

- Clinical manifestations (UMN signs and LMN signs in three regions)
- Electromyography (EMG) and nerve conduction studies
- Magnetic Resonance Spectrography (MRS)

- Cerebrospinal fluid analysis (CSF) (8)
- Muscle biopsy (5)
- DNA assay (4)

ALS patients received the following treatment

1/2000	MANAGE V	N of Patients	(%)
Glutanate antagonists	Rilutek/Riluzole	25	40
Antioxidants	Vitamin E,	42	68
	Creatine	28	45
	Selenium,	14	23
223	Coenzyme Q10	23	37
548.7	Brain-derived neurotrophic factor	4	6
2 Men > 2	Interferon	8	12
2000	Baclofen	39	62
W- 15 B	Carbocisteine	14	23
100 100 100	Amitriptyline	22	35

Classification of ESC-treated ALS patients by duration of the disease

Years	Number of Patients	Percentage (%)
Less than 1 year	10	16
Less than 2 years	19	31
Less than 3 years	29	47
More than 3 years	4	6
Total:	62	100

Classification of ESC-treated ALS patients by clinical forms

	WORLD ST.	Number Patients	of	%
1	Classical ALS (involvement of upper and lower motor neurons)	30		49
2	Primary lateral sclerosis (involvement of upper motor neurons only)	2	ij	3
3	Progressive bulbar palsy (degeneration of lower motor neurons: dysarthria, dysphonia, affected chewing and swallowing)	12	P	19
4	Progressive muscular atrophy (degeneration of lower motor neurons)	4	î	7
Co	mbined form (1+3) - 5; (4+3) - 2	7		11
Fa	mily ALS	7		- 11
Co	mbination with other autoimmune diseases:	5	1	1. 49
	Non-specific ulcerative colitis	1	я	3.77
	Psoriasis	1		Famous
	Rheumatoid arthritis	1		10041
Te	tal	62		100

Classification of ESC-treated ALS patients by predominant neurological symptoms

Form	Number of Patients	%
Bulbar	12	19
Cervicothoracic	29	47
Lumbosacral	14	23
Combined	7	11
Total:	62	100

SMEARS OF CELL USPENSION CONTAINING MESENCHYMAL EMBRYONIC CELLS. CLEAR IMAGES OF MONONUCLEAR CELLS



SYNDROME OF EARLY POST-TRANSPLANT IMPROVEMENT

I stage of EC-suspension effect - suspension stage

in 12-24 hours after transplantation; develops duration by 42 patients (67%) as:

Clear end of this period was reported by 27 patients (44%), the in criterion being emotional

(described by Alexander I. Smikodub in 1993)

Number of Patients	%
33	54
16	26
25	41
17	27
20	32
21	34
	Patients 33 16 25 17 20

Main Symptoms of Bulbar ALS in Post-Transplant Period

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Dysphonia	1	2	1		2	2	Г	П	Т	2	4		П	5.	1	П			6	2	П	1	5	2	П	П	П	1	Г	Г	г	t
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Chewing dysfunction	3	1			4				4	2			8	1			5	2	1		4	2	2	2			1				1	İ
Dysphagia	3	1		П	4	Г	П	П	3	2	1		4	2	П	Г	П	3	4	1	Г	4	3	1	П	Г	П	1	Г	Г	Г	Ī
Regargitation of liquid food	4				4				4	2			5	1				1	2			2	6					1	Г			Ī
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Main Symptoms of Classical ALS in Post-Transplant Period

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	П		Len	thus	l ye	ar-	(9)		П	b	on t	han 2	yea	n-	(11)		Г	Le	na (I	an 2	yez	9-1	(15)		Г		01	er3;	ean-	-6	B)	
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Wrist Atrophy		4	2		1	5			2	4	5		3	5	3		2	2	1		3	1		1			1	2		Ī	1	2
Atrophy of LE	3	3			3	3		П	Γ	1	6	4		2	5	4		1	6	K		1	6	8						Γ		
ROM in the wrists	1	3	2		2	4		Г	Г	4	5	2		5	3	3		1	4	1 0		2	4	9		Γ	1	2		1		2
ROM in UE	3	3	Г		5	1		Г		4	4	3		7	1	3		2	2	1		2	2	1		Г	1	2		T	1	2
ROM in LE	2	2	2		3	3	Г		Т	2	5	4	Т	4	3	4		1	6	К	П	1	6	8	П	П	2	1		1	1	1
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Spartic parrois of LE	Г	3	3		2	4	Г		2	3	3	3	2	4	4	1	2	Г	8	5	2	2	8	3	Г	Γ	3			1	2	
Weakness	П	2	4		4	2	П		т	2	5	4	Т	4	4	1	П	2	4	9	П	9	5.	6	Т	г	2	1		ь	τ	1

Terms of observation	Norm HCAB	On addenition	Before the transplantation	Alter I weeks	After I month	After 2 months	After 6 month
		11	п	- 11	- 11	10	,
B-lymphocytes CB29+, x39/1	0,21140,08	0,1940,83	0,3344,83	0,38+0,12*	0,3240,68	0,3140,06	6,3848,361
T-lymphacytes CB3+, x3F%	1,3416,02	0,3410,86	0,2940,07	9,9249,181	9,8346,17	3,1840,271	0,4540,07
T-holpers CD4+, LHF0	0,8640,01	0,4310,30	0,4910,33	0,6610,14*	0,5910,12	9,8410,14*	0,3210,09
T-suppresson CD0+, s1F0	0,5210,01	0,2510,84	0,2248,84	4,5340,16*	0,4710,35	9,7410,351	0,2240,01
NK-natural lifters CD36+, s3950	0,7116,01	0,3510,85	0,2240,85	6,3440,12	0,3410,09	8,4210,16	0,3010,08
Melper-suppressor ratio, CD4+(CD4+	1,3416,02	1,5310,28	1,01100,43	1,2410,391	1,2510,27	1,3648,2	1,4510,41
Leakecytes, cHM	1,040	4,810,53	5,411,1	6,240,76	6,841,2	5,212,3	4,911,6*
Lymphorytos, %	19-01	12,216,3	15,015,0	22,415,8	29,017,8	29,415,4	31,817,2
Absolute lymphocytes, 1970	1,3-3,6	0,5810,38	0,0510,4	1,3910,43	1,7410,37	1,5210,27	1,6219,68*

ALS Dynamics in ESC-treated Patients

After	4 months	5 months	6 months	12 months
Number of Patients	27%	42%	58%	83%

Appravation of condition by increasing:	II course of treat
- weakness.	12,8±4,3 months:
- fasciculations,	III course of trea
- local atrophies,	10,6±3,9 months;
- spasticity.	IV course of treat
- paraparesis advancement,	9,2±4,1 months;

II course of treatn	ment: -	24 /	patients afte
12,8±4,3 months;			
III course of treat	ment -	8 p	atients after
10,6±3,9 months;			
IV course of treats	ment -	3 pc	utients after
9,2±4,1 months;			
Alive (duration):	5 years		2 patients
	4 years		5 patients
	3 years		8 patients



Percentage Evaluation of Muscle Weakness (paresis grade) in Post-Transplant Period (3 months)

		D	aration of the dis	raseNumber of	patients (16)			
Evaluated muscle groups	Less than I year - (5)		Less than 2 years - (6)		Less than 3 years - (3)		Over 3 years - (2)	
Upper Extremities	R (%)	L (%)	R (%)	L(%)	R (%)	L (%)	R (%)	L(%)
Shoulder: flexors	48	32	18	21	48	42		
Shoulder: estemors	36	28	22	14	44	35	-	
Wrist: dynamometry	26	25	17	12	2	3	-	
Wrist: bandshake force	29	22	19	24	12	10	-	
	7	1	and.		11-16-3			
Lover Extremities	R (%)	L (%)	R (%)	L(%)	R (%)	L (%)	R (%)	L (%
Hip: Sexors	22	16	32	31	01			
Hig: extensors	19	18	24	25	01		-	-
Foot: flexors	*		23	21				-
Foot: Extenses	14	12	21	19	1007			-

Patient Mr. C. Letter from: 6.03.2001

irst I fell and broke a bone right below my shoulder ball joint on my left arm the 1St of this month. I had it operated on and they put a plate and 5b screws in it. Looks like the stem cells built some muscle I in the left arm it looks like it used to before the ALS worked on it... I can still walk at a normal speed and step till I get tired.