

EMBRYONIC STEM CELL TRANSPLANTATION IN DIABETES MELLITUS

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Developed was method of Embryonic Stem Cell Transplantation (without pancreas β -cells) for treatment of diabetes mellitus (DM) that proved to be effective in DM types I and II and is protected by a number of patents and is patent pending in the U.S.

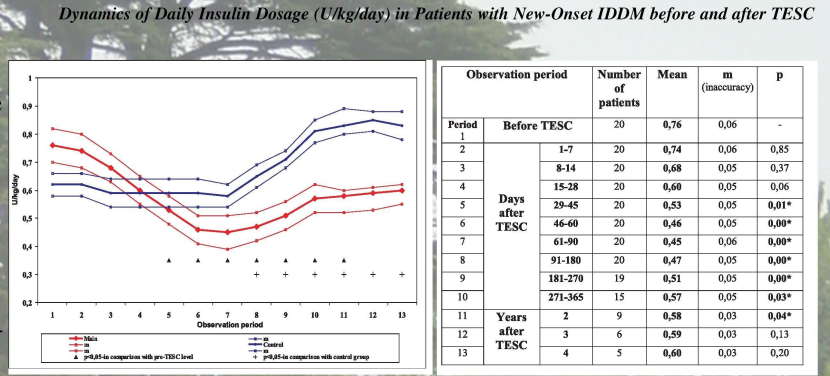
Embryonic Stem Cell Transplantation (TESC) is indicated at all stages of diabetes, being the most effective in the following cases:

- new-onset insulin-dependent DM (IDDM);
- DM complicated by diabetic nephropathy, chronic renal insufficiency (stages I and II), and anemia;
- brittle DM;
- DM complicated by infections and impaired immunity;
- non-healing trophic ulcers of soft tissues;
- secondary sulfanilamide resistance and necessity of insulin-therapy for type II DM patients.

Major Effects of Embryonic Stem Cell Transplantation

Decrease of glycemia in new-onset IDDM

In all cases, noted was gradual decrease of insulin dosages (ID) in 2-3 months after TESC. The average initial ID was $0,76 \pm 0,06$ U/kg/day. Maximum decrease amounted to 20-100% of the initial dosage (mean 41%), the term ranging from 14 to 90 days (mean $59,0 \pm 4,3$). In 65% of cases, achieved was clinical remission (daily ID $< 0,4$ U/kg/day or discontinuance) lasting 5-14 months.



Increase of endogenous insulin production

50-200% increase of serum C-peptide within one year after TESC.

Early Post-Transplantation Improvements of General State

Syndrome of Early Post-Transplantation Improvements - decreased weakness, improved workability, appetite, and sleep - was reported in 63% of cases on the first day after TESC. It was very vivid for a period of 1 month, after which its slightly reduced manifestations were maintained for 2-4 months.

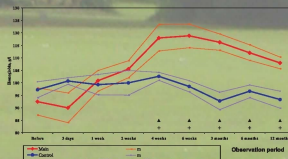
Improvement of Psycho-Physiological State

Syndrome of Psycho-Physiological Changes - improvement of physical and mental activity, decreased manifestations of depression - was observed in 48% of cases and lasted for 6-8 months.

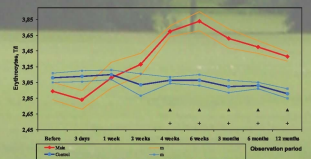
Restoration of Hematopoiesis

Restoration of hematopoiesis in diabetic nephropathy complicated by chronic renal insufficiency (stages I-II), and anemia. Reliable increase of erythrocyte count and hemoglobin in 1-1,5 months after TESC.

Hemoglobin in Patients with Diabetic Nephropathy, Chronic Renal Insufficiency, Stage I, before and after TESC



Erythrocyte Count in Patients with Diabetic Nephropathy, Chronic Renal Insufficiency, Stage I, before and after TESC



The above effects were maintained for 2-11 months.

Restoration of Immunity

Increased counts of lymphocytes, T-lymphocytes, and sub-populations of T-lymphocytes and decreased (by mean 30-60%) B-lymphocyte count were maintained for 3-8 months.

Dynamics of Immune Indices in Patients with New-Onset IDDM

Indices	Healthy TESC	Before TESC				Observation period after TESC (days)					
		n=20	m	m	p	28-45	46-60	60-90	90-90		
Lymphocytes, $\times 10^9/l$		2,06	0,21	1,23	0,11	1,64	0,09	0,0109	1,44	0,09	0,165
T-lymphocytes CD3+ $\times 10^9/l$		1,34	0,02	0,78	0,07	1,13	0,07	0,002*	0,97	0,06	0,052
%		60,94	1,49	64,0	2,2	68,8	2,2	0,151	68,2	1,6	0,169
T-helpers CD4+ $\times 10^9/l$		0,86	0,01	0,43	0,05	0,59	0,05	0,048*	0,54	0,04	0,119
%		38,55	0,84	34,6	1,9	35,5	2,0	0,731	36,8	2,7	0,499
T-suppressors CD8+ $\times 10^9/l$		0,52	0,01	0,30	0,02	0,49	0,04	0,001*	0,43	0,04	0,010*
%		23,89	2,01	25,8	2,4	29,6	1,4	0,201	30,1	1,5	0,162
T-helpers/T-suppressors ratio		1,63	0,24	1,50	0,18	1,22	0,07	0,182	1,26	0,12	0,312
B-lymphocytes CD19+ $\times 10^9/l$		0,17	0,08	0,19	0,03	0,15	0,01	0,178	0,12	0,02	0,026*
%		8,14	1,14	15,4	1,2	9,1	0,6	0,000*	8,6	0,9	0,000*

Note: p - in comparison with pre-TESC level

Dynamics of Immune Indices in Patients with Diabetic Nephropathy, Chronic Renal Insufficiency, Stage I

Indices	Healthy	Before TESC	Observation period after TESC (days)									
			n=5	m	m	p						
Lymphocytes $\times 10^9/l$		2,06	0,21	1,17	0,10	1,75	0,06	0,001*	1,75	0,09	0,001*	
T-lymphocytes CD3+ $\times 10^9/l$		1,34	0,02	0,70	0,07	1,18	0,04	0,000*	1,27	0,10	0,001*	
%		60,94	1,49	59,4	1,1	68,9	2,8	0,016*	71,3	3,5	0,013*	
T-helpers CD4+ $\times 10^9/l$		0,86	0,01	0,42	0,04	0,67	0,03	0,001*	0,72	0,04	0,001*	
%		38,55	0,84	36,2	3,3	39,1	2,1	0,497	40,9	1,2	0,228	
T-suppressors CD8+ $\times 10^9/l$		0,52	0,01	0,29	0,05	0,52	0,04	0,008*	0,54	0,09	0,048*	
%		23,89	2,01	25,3	2,3	30,4	2,2	0,162	29,4	2,8	0,304	
T-helpers/T-suppressors ratio		1,63	0,24	1,46	0,15	1,30	0,10	0,422	1,46	0,15	0,100	
B-lymphocytes CD19+ $\times 10^9/l$		0,17	0,08	0,14	0,02	0,11	0,02	0,435	0,09	0,02	0,119	
%		8,14	1,14	11,5	0,8	6,4	1,3	0,013*	5,3	0,7	0,001*	
IgA		g/l	2,52	0,42	3,51	0,54	3,11	0,34	5,51	3,16	0,44	0,633
IgG		g/l	11,42	1,32	12,72	0,69	11,63	0,83	13,49	10,41	0,80	0,062
IgM		g/l	1,28	0,09	1,87	0,23	1,81	0,23	0,868	1,60	0,09	0,339

Dystrophic Disorders and Lesions

Disappearance of trophic ulcers, decreased manifestations of skin lipidosis, diabetic foot, infectious and mycotic dermatopathies, cutaneous lichenification, and lipoatrophic lesions.

Strong effects were achieved in new-onset diabetes mellitus where Embryonic Stem Cell Transplantation proves to stop autoimmune aggression against pancreatic β -cells.

Embryonic Stem Cell Transplantation is effective in diabetes mellitus, and, as we believe, will soon become as important as insulin-therapy.