

Multiple injections with autologous mesenchymal stem cells (MSC) in patients with progressive forms of Multiple sclerosis: a long term open trial

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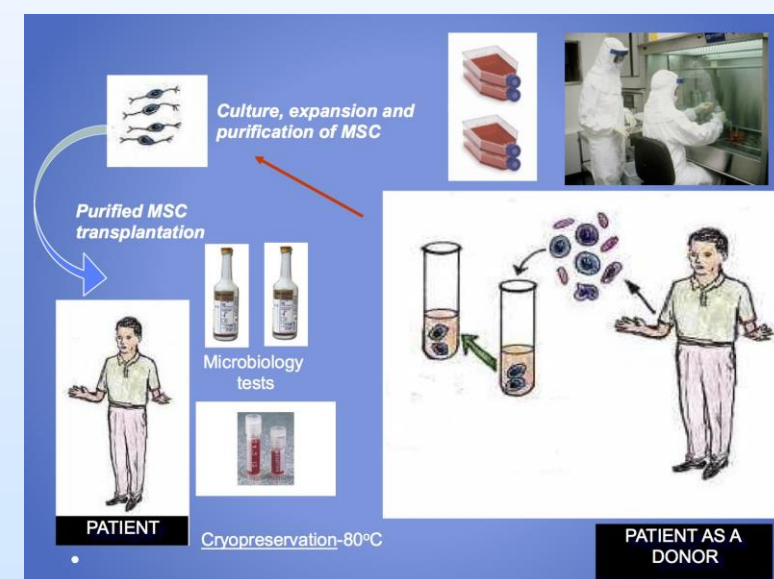


Background

Mesenchymal bone marrow derived stromal stem cells (MSC) were shown to possess immunomodulatory, neuroprotective and neurotrophic effects and due to these, they are currently used in clinical trials in multiple sclerosis (MS). In our previous pilot trial we have shown that intrathecal administration of MSC was safe and provided some indications of potentially clinically meaningful beneficial effects on the progression of the disease.

Objectives

To evaluate the long term safety of multiple injections of MSC in Multiple sclerosis.



Methods

This is an open prospective study with multiple intrathecal injections of autologous MSC in 28 patients with progressive forms of MS (either secondary progressive or relapsing-progressive course), with severe clinical deterioration and failure to respond to first and second line immunomodulatory treatments. All patients had deteriorated (at least 0.5-1 degree in the EDSS scale) during the year preceding their inclusion to our study, or had at least one major relapse without sufficient recovery following steroids treatment.

Demographics	
mean age	56.2± 14.8
mean EDSS	6.76± 1.08
mean disease duration	15.4± 6.8
MSC dose	1 million cells/kg
number of injections	min 2 to max 9
max follow up period	6 years

Number of injections	Number of treated patients
2	8 pts
3	9 pts
4	3 pts
5	2 pts
6	2 pts
8	2 pts
9	1 pts

Side effects

Transient encephalopathy	2
Hallucinations	1
Depression	1
Fever	4
Headache	4
Neck rigidity	1
Back pain	1

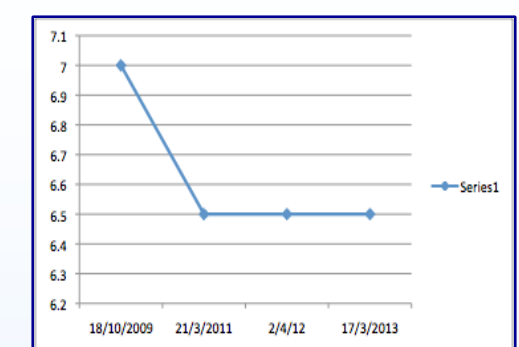
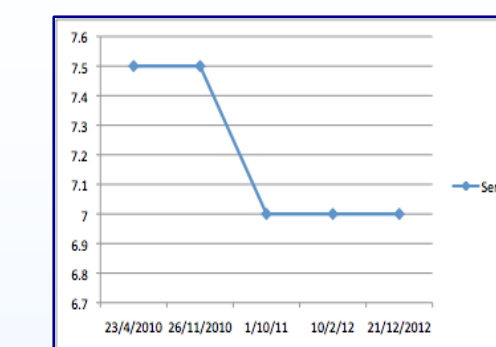
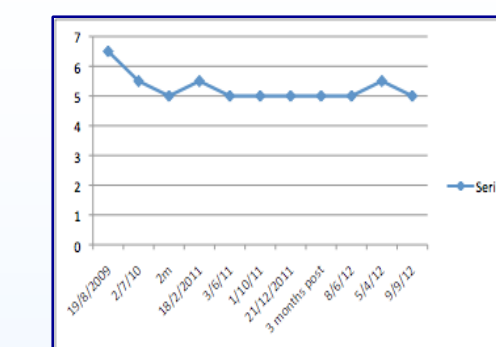
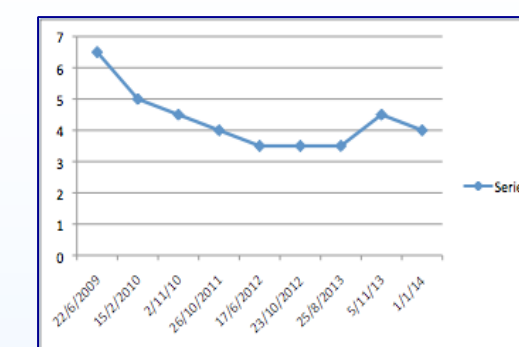
No serious side effects observed after repeated IT MSC injections in long term follow up.

Results

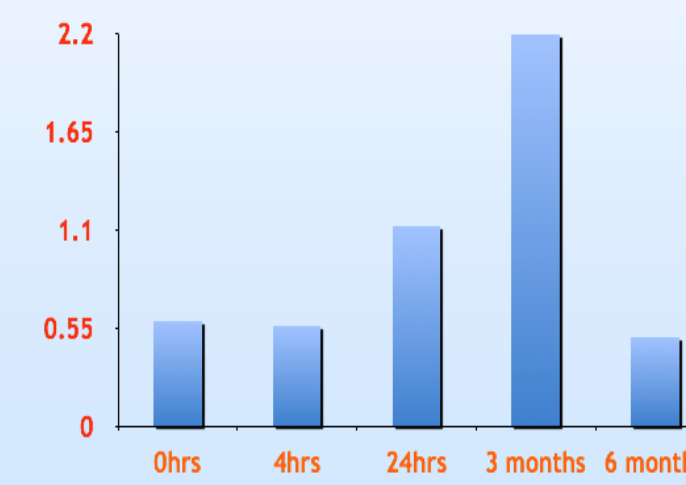
Patient	EDSS	No injections	Years of follow up	Outcome
B-I	8.0	5	2	stable
P-A	6.5	3	2	stable
R-T	6.0-6.5	3	3	deteriorated
S-E	6.0	4	3	stable
L-B	6.5-3.5	8	5	improved
G-A	6.5-5.0	9	4	improved
M-E	7.0-6.5	4	4	improved
M-S	6.5-6.0	8	5	improved
V-G	7.5	3	5	stable
S-D	7.5	4	5	stable
A-S	6.5	3	5	stable
P-T	7.0	2	3	stable
M-C	6.0-5.0	5	6	improved
S-D	7.5-7.0	5	5	improved
S-H	5.5	2	2	stable
V-P	7.5	3	4	stable
T-C	7.5-7.0	3	3	improved
T-C	5.5-5.0	2	3	stable
K-S	5.5	2	2	stable
B-E	6.5-5.5	3	3	improved
K-R	8.5	2	4	stable
I-O	8.0	3	6	stable
P-H	5.5-6.5	3	2	deteriorated
H-G	7.5	2	2	stable

25 of the 28 patients were either stable or improved in the EDSS score. The mean EDSS score reduced to 6.57± 1.8 (range: 4.5-8.5) during a mean follow up period of 3.6 years (range: 2-6). Seventeen patients were improved in at least one functional score of EDSS (14 in motor function, 5 in speech/bulbar functions, 4 in urinary functions, 6 in cerebellar function) and eight patients remained stable during all the years of follow up.

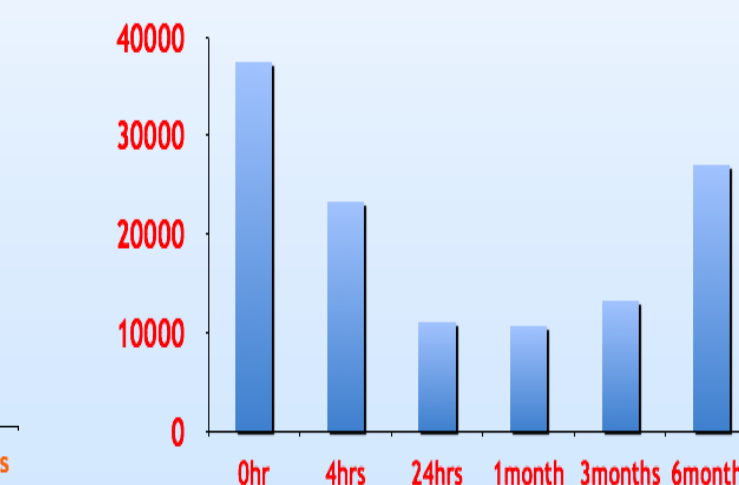
Selected MS patients receiving multiple treatments with MSC



Immunological follow up



CD4+/CD25+



Lymphocytes proliferation

Transient upregulation of regulatory T cells and downregulation of the proliferative ability of lymphocytes

Conclusions

Repeated intrathecal administration of MSC in patients with MS is safe and may induce accelerated beneficial effects.