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# Transplantation of Human Umbilical Cord Blood-derived Stem Cells Combined with Rehabilitation Therapy for the Treatment of Ataxia

## A Study of 30 Cases

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### Abstract

**Objective:** To research and document the clinical effects of treating hereditary ataxia using human umbilical cord blood-derived stem cells combined with rehabilitation therapy.

**Background:** Ataxia describes a group of diseases characterized by degenerative atrophy to the cerebellum, brain stem and/or spinal cord as the primary clinical manifestations and dysarthria, instability of gait, and even loss of the ability to stand or walk as the primary physical manifestations. Patients suffering from hereditary ataxia gradually become bed-bound and generally succumb to pulmonary infection as the main cause of death. Before stem cells, there were no effective routine therapies.

**Methods:** The human umbilical cord blood-derived stem cell treatments were created through isolation, purification, cultivation and passage. Stem cells were administered by intravenous infusion and intrathecal infusion (cervical puncture or lumbar puncture). "Proprioceptive Neuromuscular Facilitation" was used as auxiliary therapy. Results were compiled before and after treatment for symptoms and physical signs, Berg Balance Scale (BBS), sero-enzymology, hepatic and renal function, immunoglobulin and T-cell subsets.

**Results:** A reduction of pathological symptoms and signs was observed following treatment. The scores of BBS, CD3+CD8, CD4+CD8 and CPK after treatment all differed significantly from pre-treatment values ($P<0.05\sim0.001$). The combination of human umbilical cord blood-derived stem cell infusion and rehabilitation training is an effective form of treatment, which dramatically improve patient symptoms, physical signs and quality of life.

## Background

Ataxia describes a group of diseases characterized by degenerative atrophy to the cerebellum, brain stem and/or spinal cord as the primary clinical manifestations and dysarthria, instability of gait, and even loss of the ability to stand or walk as the primary physical manifestations. Cerebellar ataxia is the most common individually occurring ataxia, while Spinocerebellar ataxia (SCA) and Friedreich's ataxia (FRDA) are the most common hereditary forms. The classification is generally arrived at by genetic diagnosis. The disease features progressively disabling clinical manifestations. Patients notice instability of gait or dysarthria which can cause them to fall over without warning.

Gradually they lose the ability to walk, and become bed-bound, and generally succumb to pulmonary infection as the main cause of death. Before stem cells, there were no effective routine therapies. Genetic anticipation usually occurs in familial patients, with symptoms and signs getting more serious from generation to generation.

## Methods

- 30 ataxia patients were involved in the study, including 25 cases of spinocerebellar ataxia (SCA) (Type 1: 1 case, Type 2: 8 cases, Type 3: 5 cases, Type 6: 4 cases, unidentified genotypes: 7 cases) and 5 cases of Friedreich's ataxia (FRDA).

- Each patient received 4~6 umbilical cord blood-derived stem cell (provided by Beike Biotechnology Co., Ltd.) transplantations at intervals of 5~7 days. Stem cells were administered by intrathecal infusion (cervical puncture or lumbar puncture) into the cavitas subarachnoidealis and intravenous infusion. The quantity of cells in each transfusion was approximately 1.5~3.0×107/ml.

- During stem cell treatment, rehabilitation cycles of balance training were given twice daily for 4~6 weeks, each time lasting 30 minutes. These featured proprioceptive neuromuscular facilitation based on: (1) visual compensation, which could help improve proprioceptor sensitivity; (2) using balance boards - whereby the state was from static to moving; the support tope was from stable to unstable; and eyes were from open to closed. A phased and sequenced manner was chosen based on the result of balance evaluation.

- Therapeutic effect was described in terms of the change in BBS Score after treatment: An increase of 50% or above was defined as a marked effect; an increase of 5%-49% was defined as effective; while an increases below 5% was defined as ineffective treatment.

- The samples of each test indicator were rigorously collected and delivered for examinations pre- and post-treatment. Results were analyzed with the SPSS 11.5 statistical package using the paired Student's t-test. Differences among the means were considered significant when $P<0.05$.

## Results

**Table 1**.Berg Balance Score pre- and post treatment ($x$±s)

| item | n | pre-treatment | post-treatment |
|---|---|---|---|
| Berg Score | 30 | 35.62±11.25 | 45.25±9.33* |

Notes: *P<0.005 (significant change compared with pre-treatment)

**Table 2**. Changes of Immunoglobulin pre- and post treatment ($x$±s)

| item (unit) | n | pre-treatment | post-treatment |
|---|---|---|---|
| C3 (mg/l) | 30 | 1.18±0.247 | 1.19±0.221 |
| C4 (mg/l) | 30 | 0.26±0.073 | 0.25±0.081 |
| IgG (g/l) | 30 | 9.76±3.079 | 8.09±2.357* |
| IgA (g/l) | 30 | 1.92±0.760* | 1.92±0.760* |
| IgM (g/l) | 30 | 1.05±0.711 | 1.05±0.711 |

Notes: *P<0.05 (compared with pre-treatment)

**Table 3**. Changes of T-cell pre- and post treatment ($x$±s)

| item | n | pre-treatment | post-treatment |
|---|---|---|---|
| T (%) | 30 | 78.29±8.011 | 74.85±8.588* |
| CD3+CD4 (%) | 30 | 49.07±8.531 | 44.93±9.642* |
| CD3+CD8 (%) | 30 | 23.81±7.737 | 24.71±7.737* |
| Th/Tc (%) | 30 | 2.29±0.942 | 2.02±0.815 |

Notes: *P<0.005 (significant change compared with pre-treatment)

**Table 4**. Changes of LDH and CK pre- and post treatment ($x$±s)

| item (unit) | n | pre-treatment | post-treatment |
|---|---|---|---|
| LDH (u/l) | 30 | 165.11±40.424 | 151.94±31.21 |
| CK (u/l) | 30 | 263.82±259.22 | 106.9±60.67* |

Notes: *P<0.05 (compared with pre-treatment)

## Conclusions

- After receiving umbilical cord blood-derived stem cell transplantations, the Berg Balance Scores of all 30 ataxia patients showed significant effects, which would improve their quality of life.

- Although the detected results of IgG, IgA, T cell subset, CD3+CD4 descended within normal limits, it indicated that umbilical cord blood-derived stem cells had inhibitory actions on cellular and humoral immunity.

- The decreased value of CK in the patients after treatment suggests the possibility of treating patients suffering from muscular dystrophy or subtypes of dermatomyositis, myocarditis, and mitochondrial myopathy.

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