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Extended Abstract

Translational Medicine 2015: Authorizing the efficiency of the Human Embryonic Stem Cell (hESC) therapy in cerebral palsy patients - Geeta Shroff - Nutech Mediworld

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ABSTRACT

Background: The present study evaluated the efficacy and safety of human embryonic somatic cell (hESC) therapy in patients with Cerebral Palsy (CP).

Methods: This analysis comprised patients (30 days-18 years) with predictable identification of CP. The study consisted of four treatment phases (T1, T2, T3, T4) separated by gap phases. Efficacy of hESC therapy was evaluated supported Gross Motor Function Classification Scores Expanded and Revised (GMFCS-E & R; 1-good to 5-bad).

Results: Ninety one patients were included and every one received hESC therapy in T1, 66 patients returned for T2, 38 patients for T3, and 15 patients for T4. General, 31.2% patients attained GMFCS-E & R score 1 throughout the study with dissimilar number of patients attaining GMFCS score 1 by the top of every single treatment phase (T1: 6 [6.6%]; T2: 7 [10.6%]; T3: 11 [28.9%]; and T4: 5 [33.3%]). All patients in up to two years (n=10), 2-4 years (n=10), 4-6 years (n=9), and 6- 12 years (n=8) age bracket s except one among the 5 patients within the age group of 12-18 years transitioned from GMFCSE & R score 5 to lower scores by end of T1. Most patients transitioned to GMFCS-E & R score 2 (n=34) from upper scores by end of T2. Eleven (11) patients accomplished GMFCS-E and R score 1 by end of T3. No severe adverse proceedings were perceived.

Conclusion: Use of hESC treatment in patients with CP is actual and safe. hESC therapy has established significant enhancement in GMFCS-E and R scale.

Keywords: Human embryonic stem cells, Transplantation, Cerebral palsy, GMFCS-E & R

INTRODUCTION

Cerebral palsy (CP), a number one explanation for disability among children is caused by damage to the developing brain. Consistent with the Centers of Disease Control (CDC), prevalence of CP round the world ranges from 1.5 to quite 4 per 1,000 live births. In India, the prevalence rate of CP per 100,000 population was estimated to be 282.70 (95% CI 208.43-374.82) during a cross-sectional observation study. Stem cell therapy has the potential to beat neurological impairments caused by CP. this is often achieved by their ability to exchange damaged cells of the systema nervosum. The replacement and transformation potential is higher with embryonic stem cells (ESC) as compared with other sorts of stem cells. Human embryonic stem cells (hESCs), which are obtained from early pre-implantation stage human zygote, are self-renewing cells capable of differentiating into any cell type within the physical body. This ability has led to their extensive use within the treatment of several neurodegenerative and neurological disorders. However, there's a paucity of knowledge on use of hESCs in patients with CP. This study evaluated the efficacy of hESC therapy in patients affected with CP using Gross Motor Function Classification System-Expanded and Revised (GMFCS-E & R) in patients aged up to 18 years.

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the security of hESC therapy within the treated patients was assessed in terms of adverse events (AEs) documented at any time during the course of therapy.

Materials and Methods:

The study protocol was approved by the Independent ethics panel (IEC). The institutional committee for somatic cell research and therapy of Nutech Mediworld reported the clinical study to National Apex Body. The study was conducted in accordance to the Declaration of Helsinki.

a. Cell Culture and Differentiation:

The cells are cultured and sustained as per our exclusive in-house technology during a good laboratory practice (GLP), good tissue practice (GTP) and good manufacturing practice (GMP), certified laboratory. The cell lines are freed from animal material and are chromosomally stable. Two focused cell lines, non-neuronal and neuronal were attained from one, spare, expendable, pre grafting stage zygote taken through natural in vitro fertilization (IVF) procedure with due consent.

The priming injection of a pharmaceutical composition contained about 750,000 to 80 million hESC and/or their derivatives, suspended during a volume of about 0.25-1.0 ml of sterile normal saline. It had been estimated that 1 mL of cells dosage contained 3.5×106 hESCs; therefore, 0.25 mL contained 14×105 hESCs. The concentration of the cells at the last stage was 2.5-3.5 million cells per mL. These cells were further put in storage in 1mL, 2mL, 5mL and 10mL syringes at -20°C for additional clinical usage. When required the prefilled frozen syringes were thawed by placing the syringes in between palms of the hands till they attain the blood heat before the transplantation. After this slow thawing process, they were inserted into the patient under sterilized situations. A top quality check was performed on the stored cell batches including integrity, viability and microbial contamination. The cells were considered and therefore the transplanted cells were octamer-binding transcription factor 4 positive (OCT4 +ve); CD 34 +ve; Nestin +ve; GAF +ve; NeuN +ve and transfer gene (TRA) –ve β actin +ve; β-human chorionic gonadotropin (β– HCG) +ve; alkaline phosphatase +ve; Stage-specific embryonic antigen 3 (SSEA3) +ve; NANOG +ve; SOX +ve. The classification was done by fluorescence-activated cell sorting (FACS), immunofluorescence, and polymerase chain reaction (PCR). B.

b. Statistical Analysis:

No formal sample size was intended for this study. Each case was assessed at admission or soon after admission to work out the pre-therapy status of the case. The GMFCS-E & R scores were calculated for every patient (91 cases). All patients were classified into different age groups viz ≤2 years; 2 to 4 years; 4 to six years; 6 to 12 years; and 12 to 18 years. The analysis was supported frequency or count of the cases placed in several groups. The security analyses were performed on safety population (patients who took a minimum of one dose of hSEC). All the statistical tests were conducted at 5% level of significance. Statistical analysis was implemented using SPSS 19 software (IBM Corporation, Armonk,).

RESULTS

a. Study patients:

A total of 91 patients were included within the study and every one patient was started on intensive dosing. Most patients included within the study were males (71.4%) aged up to 18 years. All 91 patients were included in T1. Of the 91 patients, 68 patients reverted for T2, 39 patients for T3, and 15 patients for T4. The amount of patients per treatment phase is illustrated. The entire treatment days in T1 were 60 days, in T2 were 30 days, in T3 were 33 days, and in T4 were 29 days. Moreover to GMFCS-E & R scores, we also examined the reasoning skills of the patients using additional parameters. The cognitive skills of all the patients was assessed by the top of T4 using 11 parameters (problem solving, following commands, smiling, recognition/awareness, eye contact, aggression, speech, feeding, toilet training, daily living skills, and defense mechanism). This assessment was done to guage the development in cognition and functional recovery of the patients.

b. Safety Evaluation: The commonly experienced AEs included body pain, diarrhea, chest congestion, streptococcal sore throat, fever, itching, and swelling. An complete of 9 patients (9/91; 9.9%) experienced AEs during T1 (swelling-1, itching-1, fever-4, throat infection-1, and chest congestion-2), 2 patients (2/66; 3%) experienced AEs during T2 (diarrhea-1, and body pain-1), no AE were reported in T4 and one patient (1/38; 2.6%) experienced AEs during T3 (diarrhea-1). No serious AEs were reported during the study.

DISCUSSION

Cerebral palsy, a nervous disorder that affects children results in compromised psychological state and motor abilities. To our knowledge, this is often the primary study to assess efficacy and safety of hESC therapy in patients with CP. the utilization of hESCs has not been clinically viable within the overdue to difficulty in harvesting these cells during a xeno free environment. At our facility, the patients got hESC therapy alongside physiotherapy. The results of this study with hESC are promising and showed improvement in considerable number of patient's assessed. Bjorgaas et al showed that children with CP are often susceptible to conduct problems, peer problems, hyperactivity, and show a prosocial behavior. Although motor function and posture problems are common among children with CP, emotional quality of life (QoL) and social well-being is affected in these children to a big extent. consistent with a questionnaire based study, the foremost important aspects of treating patients with CP included improvement in function, mobility, activity, participation, and QoL In the present study no immunosuppresants were used. The transplantation of hESCs showed no immune reaction within the patients. This might be like surrogacy wherein an entire genetic stranger is accepted within the host, grows, and is delivered by the host. hESC therapy also improved the general well-being of the patients who participated within the study. Most patients who were unable to perform daily activities as results of CP were ready to perform them with lesser effort.

CONCLUSION

The use of hESC treatment in patients with CP is operative and safe. hESC therapy has demonstrated significant improvement in GMFCS-E & R scale and most patients transitioned to a far better score after completing all the four treatment phases. The utilization of hESC therapy showed improvement in cognitive skills CP patients. However; scarcity of knowledge associated with hESC therapy and its use within the treatment of CP demands more research during this area.