Clinical Trial Protocol
Iranian Registry of Clinical Trials
26 Jun 2019

Evaluation of the efficacy of allogeneic umbilical cord derived hematopoietic and mesenchymal stem cells on developmental functions of spastic cerebral palsy patients between 4-14 years old in comparison with control group , A Clinical trial phase II

Protocol summary

Study aim
This study designed for the evaluation of safety and therapeutic effects of intrathecal hematopoietic (MNC) and mesenchymal stem cells (MSC) derived from allogenic umbilical cord in change of developmental functions of spastic cerebral Palsy (CP) in comparison with control group .

Design
Two arm parallel group , double blind , randomized controlled trial

Settings and conduct
108 cases of Spastic CP patients between 4-14 years that have our inclusion criteria will be selected and randomly divided in 3 groups of MNC and MSC derived from umbilical cord and control of no injection . The trial is double blind and the participants and clinical evaluators are unaware of study groups .

Participants/inclusion and exclusion criteria
Inclusion criteria:Diparetic and quadriparetic spastic CP between 4-14 years old and Gross motor function classification ( GMFC) between 2 -5 Erreur! Source du fichier introuvable Exclusion criteria : Other types of CP

Intervention groups
Intervention group 1: one intrathecal injection(ITI) of MNC . Intervention group 2: one ITI of MSC. Control group: without injection ,that after insertion of needle into the skin without entrance to CSF space needle withdrawn and only simulation of ITI without the awareness of the participants . All of the participants had a baseline brain neuroimaging , that will be repeated after 12 months . Patients will be evaluated by predicted scales during the 12 months and will be followed for similar rehabilitation protocol .

Main outcome variables
Motor development alteration with GMFM 66 score Change of motor function with GMFCS score Spasticity change of patients according to Ashworth scale Developmental status according to Stanford Binet test

General information

Acronym
IRCT registration information
IRCT registration number: IRCT201706176907N13 Registration date: 2017-07-12, 1396/04/21 Registration timing: prospective

Last update: 2019-05-18, 1398/02/28 Update count: 1

Registration date
2017-07-12, 1396/04/21

Registrant information
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Recruitment status
Recruitment complete

Funding source
Tehran University of Medical Sciences , Social welfare organization of Iran,Royan stem cell Technology , Hormozgun University of Medical Sciences, Stem cell iranian science and technolgy institute

Expected recruitment start date
2017-11-22, 1396/09/01
Expected recruitment end date
2018-10-23, 1397/08/01
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
Evaluation of the efficacy of allogeneic umbilical cord derived hematopoietic and mesenchymal stem cells on developmental functions of spastic cerebral palsy patients between 4-14 years old in comparison with control group. A Clinical trial phase II

Public title
Effects of umbilical cord derived stem cells injection in the treatment of children with cerebral palsy

Purpose
Treatment

Inclusion/Exclusion criteria
Inclusion criteria:
Spastic cerebral palsy (Diparetic, Quadriparetic) Ages between 4 - 14 years Gross motor function classification (GMFC) between 2 -5 No seizure disorder or with controlled seizure Evidence of definite acquired abnormal imaging findings compatible with Cerebral Palsy Informed consent taken from their parents

Exclusion criteria:
Normal brain MRI Progressive neurological diseases (for example leukodystrophy or neurometabolic disorders) Congenital Cortical malformations Toxoplasmosis Others Rubella Cytomegalovirus Hepatitis (TORCH) infections Other types of cerebral palsy including athetoid, atonic, ataxic, and mixed type Acute intercurrent infections such as Hepatitis C Virus (HCV), Hepatitis B Virus (HBV), Human Immunodeficiency Virus (HIV) Hemorrhagic diathesis Severe anemia (Hemoglobin less than 8) Ventilator dependent pulmonary diseases Renal insufficiency

Age
From 4 years old to 14 years old

Gender
Both

Phase
2

Groups that have been masked
- Participant
- Care provider

Sample size
Target sample size: 108

Randomization (investigator's opinion)
Randomized

Randomization description
The patients are randomly allocated into three groups of intervention and control using a balanced block randomization technique. To do that, they were divided into blocks of 6 and 9. All subjects randomly allocated with online randomization software to generate random-number sequences. (Sealed Envelope Ltd. 2015. Create a blocked randomization list. [Online] Available from: https://www.sealedenvelope.com/simple-randomiser/v1/lists [Accessed 15 Dec 2015]). Coordinator and Physician responsible for assessing inclusion / exclusion criteria and registering individuals are blind. Due to necessity of HLA matching of hematopoietic stem cells derived from allogenic umbilical cord (MNC) group we selected 150 cases of referred patients with our inclusion criteria and HLA analysis were done for these patients and then 36 cases of class 6 matched patients enrolled to the MNC group and 72 cases among the remaining patients randomly divided to Mesenchymal stem cells derived from allogenic umbilical cord (MSC) and control group. Therefore 108 cases enrolled in 3 divided group of 36 patients.

Blinding (investigator's opinion)
Double blinded

Blinding description
As this study designed as double blind, In the control group after insertion of the needle into the skin with an appearance of simulation of lumbar puncture no injection were done without the awareness of the patients or their parents and clinical evaluators. At the end of the study if safety and effectiveness of cell therapy will be proved for ethical consideration cell therapy will be performed for control group.

Placebo
Not used

Assignment
Parallel

Other design features
For the first time in our country, intrathecal injection of mesenchymal stem cells derived from umbilical cord for the treatment of CP applied.

Secondary Ids

1

Registry name
Clinical trials.gov

Secondary trial Id
NCT03795974

Registration date
2019-01-08, 1397/10/18

Ethics committees

1

Ethics committee
Name of ethics committee
Ethic committee of Tehran university of Medical Sciences

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Tehran University of Medical Sciences, Ghods street, Keshavarz Blvd, Tehran

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Approval date
2017-06-06, 1396/03/16

Ethics committee reference number
IR.TUMS.VCRREC.1996.2506
Health conditions studied

1 Description of health condition studied
   Spastic Cerebral Palsy

ICD-10 code
   G80.9

ICD-10 code description
   Cerebral Palsy , Unspecified

Primary outcomes

1 Description
   Motor development alteration with GMFM 66 score

Timepoint
   Before intervention , 1 month after intervention , 3 months after intervention , 6 months after intervention , 12 months after intervention

Method of measurement
   questionnaire

Secondary outcomes

1 Description
   Probable Change of brain lesions

Timepoint
   Before intervention , 1 year after intervention

Method of measurement
   Brain Magnetic Resonance Imaging (MRI) , Brain Magnetic Resonance Spectroscopy (MRS) , Brain Deep Tensor Imaging (DTI)

2 Description
   Fever

Timepoint
   24 hours after intervention , 48 hours after intervention , 72 hours after intervention

Method of measurement
   Axillary thermometer

3 Description
   Meningitis

Timepoint
   First 3 days after intervention or any time after intervention

Method of measurement
   Lumbar Puncture

4 Description
   Hyper sensitivity reactions

Timepoint
   First week after intervention

Method of measurement
   Physical exam

Intervention groups

1 Description
   Intervention group 1 one intrathecal injection of hematopoietic stem cell derived from umbilical cord ( 5 millions per Kg ) prepared by Royan stem cell Technology Company . Intrathecal injection will be done under anesthesia via lumbar puncture . After taking 5 milliliter of cerebrospinal fluid prepared stem cells will be injected with a syringe . The patient will be admitted for one day of probable adverse reaction observation . One year followup and evaluation with regular similar rehabilitative therapy will be done.

Category
   Treatment - Drugs

2 Description
   Intervention group 2 one intrathecal injection of mesenchymal stem cells derived from umbilical cord ( 1
Intrathecal injection will be done under anesthesia via lumbar puncture. After taking 5 milliliter of cerebrospinal fluid prepared stem cells will be injected with a syringe. The patient will be admitted for one day of probable adverse reaction observation. One year followup and evaluation with regular similar rehabilitative therapy will be done.

### Category

**Treatment - Drugs**

3

### Description

Control group without injection, that after insertion of needle into the skin without entering into the cerebrospinal fluid space, needle will be withdrawn without any injection and only with an appearance of simulation of lumbar puncture without the awareness of the patient or their parents. The patient will be admitted for one day of probable adverse reaction observation. One year followup and evaluation with regular similar rehabilitative therapy will be done.

### Category

**Treatment - Other**

Recruitment centers

1

**Recruitment center**

**Name of recruitment center**

Children's Medical Center Hospital

**Full name of responsible person**

Anahita Majmaa

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### Sponsors / Funding sources

1

**Sponsor**

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**Grant name**

**Grant code / Reference number**

**Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**

Tehran University of Medical Sciences

**Proportion provided by this source**

40

**Public or private sector**

Public

**Domestic or foreign origin**

Domestic

**Category of foreign source of funding**

empty

**Country of origin**

Iran (Islamic Republic of)

**Type of organization providing the funding**

Academic

2

**Sponsor**

**Name of organization / entity**

ROYAN stem cell technology Co

**Full name of responsible person**

Morteza zarrabi

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**Grant name**

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**Is the source of funding the same sponsor organization/entity?**

Yes

**Title of funding source**
ROYAN stem cell technology Co

Proportion provided by this source
30

Public or private sector
Private

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin
Type of organization providing the funding
Industry

3

Sponsor
Name of organization / entity
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Full name of responsible person
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Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
Welfare Organization of Iran

Proportion provided by this source
20

Public or private sector
Public

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin
Type of organization providing the funding
Other

4

Sponsor
Name of organization / entity
Hormozgan University of Medical Sciences

Full name of responsible person
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Grant name
Grant code / Reference number
Is the source of funding the same sponsor organization/entity?
Yes

Title of funding source
Hormozgan University of Medical Sciences

Proportion provided by this source
10

Public or private sector
Public

Domestic or foreign origin
Domestic

Category of foreign source of funding
empty

Country of origin
Type of organization providing the funding
Academic

Person responsible for general inquiries

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Sharing plan
Deidentified Individual Participant Data Set (IPD)
Yes - There is a plan to make this available
Study Protocol
Yes - There is a plan to make this available
Statistical Analysis Plan
Undecided - It is not yet known if there will be a plan to make this available
Informed Consent Form
Yes - There is a plan to make this available
Clinical Study Report
Yes - There is a plan to make this available
Analytic Code
No - There is not a plan to make this available
Data Dictionary
Not applicable
Title and more details about the data/document
IPD collected for the primary outcomes and secondary outcome measures
When the data will become available and for how long
Dec 2019
To whom data/document is available
people working in academic institutions, people working in businesses and patients
Under which criteria data/document could be used
Publications of study
From where data/document is obtainable
Contact persons
What processes are involved for a request to access data/document
Telephone or email
Comments