Chapter 9
Stem Cells in Regenerative Medicine: Clinical Trials

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Abstract Stem cells have been extensively used in tissue repair and cell tissue engineering in preclinical and clinical conditions. One of the stem cells' characteristics is to provide an ample number of cells for transplantation purposes. Although embryonic stem cells (ESCs) are considered a potential source of stem cells, due to ethical concerns, there is not much progress in using ESCs in clinical conditions. The application of adult mesenchymal stem cells (MSCs) derived from bone marrow, and the umbilical cord is extensively used to treat many degenerative diseases. Many clinical trials have been successfully done in the last few years. Moreover, many clinical trials with different phases are under progress where adult MSCs are transplanted in patients with different degenerative diseases. More than 5000 registered clinical trials are in progress as per the ClinicalTrials.gov where stem cells have been applied in disease conditions.

Keywords Stem cells therapy · Regenerative medicine · Cell therapy · Clinical trials

Introduction

Stem cell therapy, also known as regenerative medicine, promotes the repair response of diseased, dysfunctional, or injured tissue using stem cells or their derivatives. One of the main requirements for cell-based therapy is to test the cells in different phases in humans, called clinical trials. There are four different clinical trial phases, such as Phase-1, Phase-2, Phase-3, and Phase-4 trials, respectively. These clinical trials are performed in healthy persons and patients, which aim to evaluate potential benefits. Such trials' primary objectives are to find out if the cell-based therapy is safe (healthy person) and therapeutically effective (patients). Often, clinical trials are used to learn if a new cell-based therapy is more effective or has less harmful side effects. In the

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year 2014, cell-based therapies clinical trials were either sponsored by academic institutions roughly constitute 70% of total clinical trials, and 30% of clinical trials were sponsored by private companies (Bersenev, 2015). It has been observed that a combination of public and private funding was strongly encouraged in the clinical trials conducted by the Californian Institute for Regenerative Medicine, California, USA (Trounson et al., 2010). The investments for stem cell clinical trials have been heavily based on the successful and positive clinical trial results. The primary concern of any investments toward stem cell-based clinical trials is to get clear information about the trial's outcome. Over the past few years, attempts have been made to better evaluate and monitor the stem cell-based trials at different intervals. It has often been observed that investors have retracted the funding due to non-getting satisfactory trial results. The outcome of clinical trials must be shared with investors with the technical team to decide whether to continue the trials.

There have been reports on clinical trials (Ratcliffe et al., 2013; Trounson et al., 2011), where different stem cells have been used in the clinical trials. Most of the publicly available data on stem cell-based therapy trials either available at the National Institute of Health, USA, and European databases. The outcome of stem cell-based clinical trials has also been published in peer-reviewed journals, and they are available at the National Center for Biotechnology Information, USA. However, some clinical trial data are not available in the public domain. As stem cell-based therapy is a new therapy, it is essential to have the outcome of all clinical trials to be able to develop effective cell-based therapy. Among different stem cells, limbal stem cells and neural stem cells showed significant promising results in regenerative repair. The application of pluripotent stem cells and mesenchymal stem cells (MSCs) is the most widely used cell types for clinical trials. There is also interest in placental-derived stem cells in regenerative medicine. The application of stem cell-based therapy is mostly used in eye-related degenerative diseases. One of the reasons is that small numbers of cells required in the eye regeneration, and tissue is easily accessible for surgery.

Concerning the type of stem cell transplantation, autologous stem cell transplantation is most widely used as there are many benefits of using autologous transplantation such as easily accepted by the body, no immuno rejection issue, and cell survivability and functionality are better. In the case of allogeneic cell transplantation, few clinical trials are conducted, but due to high immuno rejection and low cell acceptability, allogeneic cell transplantation is less favored than autologous cell transplantation. Different types of stem cells, such as pluripotent stem cells and induced pluripotent stem cells, are extensively used in clinical trials (Cyranoski, 2014; Kushner et al., 2014; Schwartz et al., 2012, 2015).

Clinical Trials of Bone and Muscle Diseases Using Stem Cell Therapy

Stem cells have been tested as the treatment for various bone and muscle-related diseases. Many clinical trials are currently in progress or have been completed where stem cells have been used in bone and muscle disease. The summary of clinical trials is listed in the tables.

Bone Disease and Regenerative Medicine

Forty clinical trials are being performed using different types of stem cells to treat bone diseases as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The list of trial which has been conducted during the year 2009–2020 is listed in Table 9.1.

Clinical Trials in Joint Diseases and Stem Cell Therapy

As per the clinical trial record, more than 110 clinical trials are being performed using different types of stem cells to treat joint diseases as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The list of trial which has been conducted during the year 2019–2020 is listed in Table 9.2.

Musculoskeletal Disease and Stem Cell Therapy

One hundred sixty clinical trials are being conducted using different stem cells to treat musculoskeletal diseases as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The list of trial which has been conducted during the year 2020 is listed in Table 9.3.

Table 9.1 Bone disease and stem cell therapy

Title of trial	Disease	Type of stem cells	Year
Evaluation of clinical and bone density improvement after implantation of allogeneic mesenchymal stem cell from umbilical cord on osteoporosis patients	Osteoporosis	Mesenchymal stem cell	2020
Effectiveness and safety of mesenchymal stem cell (MSc) implantation on degenerative disc disease patients	Degenerative disc disease, low back pain; disc degeneration	Mesenchymal stem cell + NaCl 0.9% 2 ml	2020
Effectivity of mesenchymal stem cell on vertebral bone defect due to mycobacterium tuberculosis infection	Spinal tuberculosis	Combination product: mesenchymal stem cell + NaCl 0.9%	2020
Human umbilical cord mesenchymal stem cells for the treatment of lumbar disc degeneration disease	Lumbar disc degeneration; lumbar disc herniation	Human umbilical cord mesenchymal stem cells	2020
Efficacy in alveolar bone regeneration with autologous MSCs and biomaterial in comparison to autologous bone grafting	Alveolar bone atrophy interventions:	Advanced medicinal therapy (MSCs combined with biomaterial); procedure: autologous bone graft	2020
The study of early stage osteonecrosis of femoral head with human umbilical cord mesenchymal stem cells	Osteonecrosis of femoral head	Drug: Allogeneic umbilical cord mesenchymal stem cells	2017
Repairing the defect of intervertebral disc with autologous BMSC and gelatin sponge after microendoscopic discectomy for lumbar disc herniation	Lumbar disc herniation	Autologous bone marrow stem cell (BMSC)/gelatin sponge	2016
Interbody spacers with map3® cellular allogeneic bone graft in anterior or lateral lumbar interbody fusion	Spondylosis, degenerative disc disease	Cellular allogeneic bone graft	2015
Role of mesenchymal stem cells in fat grafting	Romberg's disease, craniofacial microsomia; lipodystrophy; mixed connective tissue disease	Fat graft enriched with ex vivo expanded stem cells, procedure: Fat graft not enriched with ex vivo expanded stem cells	2015

(continued)

Table 9.1 (continued)

Title of trial	Disease	Type of stem cells	Year
Clinical trial of intravenous infusion of fucosylated bone marrow mesenchymal cells in patients with osteoporosis	Osteoporosis, spinal fractures	Fucosylated MSC for osteoporosis	2015
Clinical trial of use of autologous bone marrow stem cells seeded on porous tricalcium phosphate matrix and demineralized bone matrix in patients with osteonecrosis	Osteonecrosis	MSC construct for osteonecrosis	2015
Autologous adipose-derived stem cell therapy for intervertebral disc degeneration	Low back pain intervention	Autologous adipose-derived mesenchymal stem cell	2015
Phase 2a study on allogeneic osteoblastic cells implantation in lumbar spinal fusion	Degenerative disc disease intervention	ALLOB® cells with ceramic scaffold	2014
Mesenchymal stem cell based therapy for the treatment of osteogenesis imperfecta	Osteogenesis imperfecta intervention	Mesenchymal stem cells	2014
Adipose cells for degenerative disc disease	Degenerative disc disease	Adipose stem cells	2014
Evaluation of mesenchymal stem cells to treat avascular necrosis of the hip	Avascular necrosis of the femoral head	Cultured autologous mesenchymal cells	2014
Autologous stem cells in achilles tendinopathy	Achilles tendinitis, degeneration	Biological: autologous mesenchymal stem cells	2014
Phase II clinical trial prospective, open, nonrandomized treatment of osteonecrosis of the femoral head by the administration of autologous mesenchymal stem cells	Osteonecrosis of the femoral head	Bone marrow aspirate	2012
Autologous adipose tissue-derived mesenchymal stem cells transplantation in patient with lumbar intervertebral disc degeneration	Lumbar intervertebral disc degeneration	Autologous adipose tissue-derived MSCs transplantation	2012

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Table 9.1 (continued)

Title of trial	Disease	Type of stem cells	Year
Mesenchymal stem cells in osteonecrosis of the femoral head	Avascular necrosis of femur head	XCEL-MT-OSTEO-ALPHA	2012
Safety study of mesenchymal stem cells and spinal fusion	Lumbar spondylolisthesis involving L4-L5, degenerative discopathy involving L4-L5	XCEL-MT-OSTEO-ALPHA	2012
Safety and efficacy study of umbilical cord/placenta-derived mesenchymal stem cells to treat ankylosing spondylitis (AS)	Ankylosing spondylitis	Human umbilical cord-derived MSCs	2011
The use of autologous bone marrow mesenchymal stem cells in the treatment of articular cartilage defects	Degenerative arthritis; chondral defects; osteochondral defects	Bone marrow mesenchymal stem cell implantation	2009

Neuromuscular Disease and Stem Cell Therapy

There are 40 clinical trials being conducted using different types of stem cells to treat neuromuscular diseases as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The trial list conducted during the year 2017–2020 is listed in Table 9.4.

Clinical Trials of Brain Diseases and Stem Cell Therapy

Stem cells have been tested as the treatment for various brain-related diseases and injuries. Many clinical trials are currently in progress or have been completed where stem cells have been used in bone and muscle disease as per the USA clinical trials portals.

Table 9.2 List of clinical trials in joint diseases

Title of trial	Disease	Type of stem cells	Year
Phase 2B clinical study of chondrogen for treatment of knee osteoarthritis	Osteoarthritis, knee	Chondrogen	2020
Autologous adipose tissue-derived mesenchymal stem cells (AdMSCs) for osteoarthritis	Osteoarthritis, knee; osteoarthritis, osteoarthritis shoulder	Biological: Celltex-AdMSCs	2020
Allogeneic BM-MSCs in patients with lumbar facet arthropathy	Facet-mediated low back pain	Single bilateral intra-articular injection of allogeneic BM-MSCs for lumbar facet joint arthropathy	2020
Bone marrow versus adipose autologous mesenchymal stem cells for the treatment of knee osteoarthritis	Osteoarthritis knee	Biological: bone marrow mesenchymal stem cells; biological: adipose Mesenchymal stem cells; biological: bone marrow and adipose mesenchymal stem cells injection	2020
Comparative effectiveness of arthroscopy and non-arthroscopy using mesenchymal stem cell therapy (MSCs) and conditioned medium for osteoarthritis	Osteoarthritis, knee	Mesenchymal stem cells with arthroscopy; biological: mesenchymal stem cells without arthroscopy	2020
Study on shoulder arthritis treatment with intra-articular injections of autologous bone marrow aspirate	Shoulder arthritis	Marrow cellution system	2020
Clinical study of intra-articular injection of catholic MASTER cell (bone marrow-derived mesenchymal stem cell) in knee osteoarthritis	Osteoarthritis, knee	Bone marrow-derived mesenchymal stem cell	2020
Adipose-derived biocellular regenerative therapy for osteoarthritis	Osteoarthritis; osteoarthritis knee; osteoarthritis shoulders; osteoarthritis of multiple joints; osteoarthritis, hip; osteoarthritis—ankle/foot	Tissue stromal vascular fraction	2020

(continued)

Table 9.2 (continued)

Title of trial	Disease	Type of stem cells	Year
Treatment of osteoarthritic knee with high tibial osteotomy and implantation of allogeneic human umbilical cord blood-derived stem cells	Osteoarthritis, knee	Umbilical cord blood stem cell implantation for osteoarthritis treatment	2020
Treatment of knee osteoarthritis with autologous adipose-derived mesenchymal stem cells	Knee osteoarthritis	Autologous adipose-derived mesenchymal stem cells	2019
Clinical study of pulp mesenchymal stem cells in the treatment of primary mild to moderate knee osteoarthritis	Knee osteoarthritis	Mesenchymal stem cell	2019
The evaluation of safety and effectiveness of intra-articular administration of autologous stromal vascular fraction of adipose tissue cells for treatment of knee joint arthritis	Knee osteoarthritis intervention	Stromal vascular fraction	2019
Mesenchymal stem cell transplantation for osteoarthritis	Knee osteoarthritis	Autologous BMSCs plus autologous PRP	2019
Treatment of early knee osteoarthritis with autologous adipose-derived mesenchymal stem cells	Knee osteoarthritis	Autologous adipose-derived mesenchymal stem cells	2019
Effectiveness of autologous adipose-derived stem cells in the treatment of knee cartilage injury	Knee osteoarthritis; cartilage degeneration	Autologous adipose-derived mesenchymal stem cell	2019
Multicenter trial of stem Cell Therapy for osteoarthritis (MILES)	Osteoarthritis	Autologous bone marrow concentrate biological: adipose-derived stromal vascular fraction (SVF); biological: umbilical cord tissue (UCT)	2019
Implantation of allogeneic mesenchymal stem cell from umbilical cord blood for osteoarthritis management	Osteoarthritis, knee	Umbilical cord mesenchymal stem cell; biological: recombinant human somatropin	2019

Table 9.3 List of clinical trials in musculoskeletal disease

Title of trial	Disease	Type of stem cells	Year
Evaluation of clinical and bone density improvement after implantation of allogeneic mesenchymal stem cell from umbilical cord on osteoporosis patients	Osteoporosis	Mesenchymal stem cell	2020
Human umbilical cord mesenchymal stem cells for the treatment of lumbar disc degeneration disease	Lumbar disc degeneration; lumbar disc herniation	Human umbilical cord mesenchymal stem cells	2020
Allogeneic BM-MSCs in patients with lumbar facet arthropathy	Facet-mediated low back pain	Single bilateral intra-articular injection of allogeneic BM-MSCs for lumbar facet joint arthropathy	2020
Bone marrow versus adipose autologous mesenchymal stem cells for the treatment of knee osteoarthritis	Condition: osteoarthritis knee injection	Bone marrow mesenchymal stem cells; biological: adipose mesenchymal stem cells; biological: bone marrow and adipose mesenchymal stem cells injection	2020
Comparative effectiveness of arthroscopy and non-arthroscopy using mesenchymal stem cell therapy (MSCs) and conditioned medium for osteoarthritis	Osteoarthritis, knee	Mesenchymal stem cells	2020
Efficacy in alveolar bone regeneration with autologous MSCs and biomaterial in comparison to autologous bone grafting	Alveolar bone atrophy	Advanced medicinal therapy (MSC combined with biomaterial); Autologous bone graft	2020
Treatment of osteoarthritic knee with high tibial osteotomy and implantation of allogeneic human umbilical cord blood-derived stem cells	Osteoarthritis, knee	Umbilical cord blood stem cell implantation for osteoarthritis treatment	2020

Table 9.4 List of clinical trials in neuromuscular diseases

Title of trial	Disease	Type of stem cells	Year
Evaluation of clinical and bone density improvement after implantation of allogeneic mesenchymal stem cell from umbilical cord on osteoporosis patients	Osteoporosis	Mesenchymal stem cell	2020
BMAC nerve allograft study	Peripheral nerve injury upper limb	Nerve graft with autologous BMAC	2019
In vivo analysis of muscle stem cells in chronic and acute lower limb ischemia (MyostemIschemia)	Conditions: artery disease; muscle disorder	Gastrocnemius muscle biopsy	2019
A study to evaluate transplantation of astrocytes derived from human embryonic stem cells, in patients with amyotrophic lateral sclerosis (ALS)	Condition: ALS (amyotrophic lateral sclerosis)	Astrocytes derived from human embryonic stem cells	2018
Intrathecal autologous adipose-derived mesenchymal stromal cells for amyotrophic lateral sclerosis (ALS)	ALS; amyotrophic lateral sclerosis	Autologous adipose-derived mesenchymal stromal cells	2017
Safety/efficacy study of 2nd cycle treatment after 6 months of 1st cycle HLA-haplo matched allogeneic bone marrow-derived stem cell treatment in ALS	Amyotrophic lateral sclerosis	Bone marrow-derived stem cell	2017
Safety assessment of intravitreal mesenchymal stem cells for acute non-arteritic anterior ischemic optic neuropathy	Non-arteritic ischemic optic neuropathy	Intravitreal mesenchymal stem cells	2017
Bone marrow-derived autologous stem cells for the treatment of Duchenne muscular dystrophy	Duchenne muscular dystrophy	Bone marrow-derived autologous stem cells	2017
Adipose stem/stromal cells in RSD, CRPS, fibromyalgia	RSD (reflex sympathetic dystrophy); CRPS—complex regional pain syndrome type I; fibromyalgia	Adipose stem/stromal cells	2017

List of Clinical Trials in Brain Injuries

Forty-six clinical trials are being conducted using different types of stem cells to treat brain injuries as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The trial list conducted during the year 2017–2020 is listed in Table 9.5.

List of Clinical Trials in Brain Diseases

One hundred ten clinical trials are being conducted using different types of stem cells to treat brain diseases as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-tri

Table 9.5 List of clinical trials in brain injuries

Title of trial	Disease	Type of stem cells	Year
Study of the therapeutic effects of cortical autograft implantation in patients with cerebral ischemia	Condition: ischemic stroke	Autologous transplant	2020
Stem cell and conditioned medium for cerebral palsy	Condition: cerebral palsy	Umbilical cord mesenchymal stem cells	2020
Clinical effect and safety of autologous umbilical cord blood transfusion in the treatment of cerebral palsy	Cerebral palsy	Autologous umbilical cord blood transfusion	2019
Alzheimer's autism and cognitive impairment stem cell treatment study	Alzheimer's autism and cognitive impairment	Intravenous bone marrow stem cell (BMSC) fraction	2018
The treatment of premature infants with brain injury by autologous umbilical cord blood stem cells	Premature infants with brain injury	Autologous umbilical cord blood stem cells	2018
Transplantation of umbilical cord-derived mesenchymal stem cells via different routes	Cerebral palsy	Umbilical cord-derived mesenchymal stem cells	2018
Allogeneic mesenchymal stem cell-derived exosome in patients with acute ischemic stroke	Acute ischemic stroke	Allogeneic mesenchymal stem cell-derived exosome	2018
Mechanism of allogeneic UCB therapy in cerebral palsy	Cerebral palsy	Allogeneic cord blood transplantation	2017

Table 9.6 List of clinical trials in brain diseases

Title of trial	Disease	Type of stem cells	Year
Evaluate the safety and explore efficacy of umbilical cord mesenchymal stem cells in acute ischemic stroke	Acute ischemic stroke	Umbilical cord mesenchymal stem cells	2020
Stereotactic transplantation of hAESCs for Parkinson's disease	Parkinson's disease	Human amniotic epithelial stem cells	2020
The safety and the efficacy evaluation of allogeneic adipose MSC-Exos in patients with Alzheimer's disease	Alzheimer's disease	Allogeneic adipose MSC-exosomes	2020
Stem cell and conditioned medium for cerebral palsy	Cerebral palsy	Umbilical cord mesenchymal stem cells	2020
Allogeneic adipose tissue-derived mesenchymal stem cells in ischemic stroke	Ischemic stroke	Allogeneic adipose tissue-derived stem cells	2020
Mesenchymal stem cells for the treatment of acute ischemic stroke	Acute ischemic stroke	Mesenchymal stem cells	2019
Effect of different transplantation time for mesenchymal stem cells(MSCs) of cerebral infarction patients	Cerebral infarction, ischemic; acute stroke	Effect of different transplantation time for mesenchymal stem cells (MSCs) o	2019
An open-labeled phase ii study to evaluate the efficacy and safety of GXNPC-1 (Autologous adipose-derived stem cells) in patients with chronic stroke	Chronic stroke	Autologous adipose-derived stem cells	2019
Alzheimer's disease stem cells multiple infusions	Alzheimer's disease	Stem cells multiple infusions; 100 million cells allogeneic hMSC	2019
Effects of growth hormone and IGF-1 on anabolic signals and stem cell recruitment in human skeletal muscle	Growth hormone deficiency	Effects of Growth Hormone and IGF-1 + Stem Cell recruitment	2019
A study on the treatment of Parkinson's disease with autologous neural stem cells	Parkinson disease	Autologous neural stem cells	2019

(continued)

Table 9.6 (continued)

Title of trial	Disease	Type of stem cells	Year
Clinical effect and safety of autologous umbilical cord blood transfusion in the treatment of cerebral palsy	Cerebral palsy	Autologous umbilical cord blood transfusion	2019
Alzheimer's autism and cognitive impairment stem cell treatment study	Alzheimer's autism and cognitive impairment	Intranasal topical bone marrow stem cell	2018
The treatment of premature infants with brain injury by autologous umbilical cord blood stem cells	Infants with brain injury	Autologous umbilical cord blood stem cells	2018
Use of mesenchymal stem cells in Parkinson disease (PD)	Parkinson disease (PD)	Mesenchymal stem cells—umbilical cord-derived MSCs	2018
Investigation of neural stem cells in ischemic stroke	Ischemic stroke, chronic stroke	Neural stem cells	2018
Regenerative stem cell therapy for stroke in Europe 1 ()	Stroke	Stem cell therapy—adipose-derived stem cell	2018
Umbilical cord-derived mesenchymal stem cells therapy in Parkinson's disease	Parkinson's disease	Umbilical cord-derived mesenchymal stem cells therapy	2018
MultiStem® administration for stroke treatment and enhanced recovery study	Ischemic stroke	MultiStem®	2018
Study of UCB and MSCs in children with CP: ACCeNT-CP	Children with cerebral palsy	Allogeneic umbilical cord blood	2018
Transplantation of umbilical cord-derived mesenchymal stem cells via different routes	Cerebral palsy	Transplantation of umbilical cord-derived mesenchymal stem cells	2018
Allogeneic mesenchymal stem cell-derived exosome in patients with acute ischemic stroke	Acute ischemic stroke Condition: cerebrovascular disorders	Allogeneic mesenchymal stem cell-derived exosome	2017
Umbilical cord mesenchymal stem cells therapy for patients with spinocerebellar ataxia	Patients with spinocerebellar ataxia	Umbilical cord mesenchymal stem cells therapy	2017
Mesenchymal stem cells therapy in patients with recent intracerebral hemorrhage	Hemorrhagic stroke; intracerebral hemorrhage	Mesenchymal stem cells therapy	2017

(continued)

Table 9.6 (continued)

Title of trial	Disease	Type of stem cells	Year
Transplantation of neural stem cell-derived neurons for Parkinson's disease	Parkinson's disease	Transplantation of neural stem cell-derived neurons—intracerebral microinjections	2017
The safety and efficacy of human umbilical cord mesenchymal stem cells in the treatment of acute cerebral infarction	Cerebral infarction	Human umbilical cord mesenchymal stem cells	2017
Follow-up study of safety and efficacy in subjects who completed NEUROSTEM® Phase-I/IIa Clinical Trial Condition: Alzheimer's disease	Alzheimer's disease	NEUROSTEM® Phase-I/IIa clinical human umbilical cord blood-derived mesenchymal stem cells	2017
Human umbilical cord mesenchymal stem cell therapy for cerebral infarction patients in convalescent period	Cerebral infarction	Human umbilical cord mesenchymal stem cell therapy—allogeneic umbilical cord mesenchymal stem cell	2017
Safety and efficacy study of human ESC-derived neural precursor cells in the treatment of Parkinson's disease	Parkinson's disease	Human ESC-derived Neural precursor cells	2017
Stem cells in umbilical blood infusion for cerebral palsy	Cerebral palsy	Stem cells in umbilical blood infusion	2017
A study to evaluate the safety and efficacy of human neural stem cells for Parkinson's disease patient	Parkinson disease	Human neural stem cells	2017

als-portal). The list of trial which has been conducted during the year 2017–2020 is listed in Table 9.6.

List of Clinical Trials in Spinal Cord Injuries

Fifty-two clinical trials are being conducted using different types of stem cells to treat brain diseases as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The trial list conducted during the year 2016–2020 is listed in Table 9.7.

Table 9.7 List of clinical trials in spinal cord injuries

Title of trial	Disease	Type of stem cells	Year
Autologous bone marrow-derived mononuclear cells for acute spinal cord injury	Spinal cord injury	Autologous bone marrow-derived mononuclear cells	2020
Autologous adipose-derived mesenchymal stem cells for spinal cord injury patients	Spinal cord injuries; paralysis	Autologous adipose-derived mesenchymal stem cells	2020
Treatment of spinal cord injuries with (AutoBM-MSCs) versus (WJMSCs)	Spinal cord injuries	Autologous bone marrow-MSCs	2020
Safety stem cells in spinal cord injury	Spinal cord injuries	Safety stem cells	2019
Umbilical cord blood cell transplant into injured spinal cord with lithium carbonate or placebo followed by locomotor training	Spinal cord injuries	Umbilical cord blood cell transplant	2019
Clinical study of an autologous stem cell product in patients with a (Sub)acute spinal cord injury	Spinal cord injuries	Autologous stem cell	2019
Intrathecal transplantation of UC-MSC in patients with early stage of chronic spinal cord injury	Spinal cord injuries	Intrathecal transplantation of umbilical cord-MSC	2018
Intrathecal transplantation of UC-MSC in patients with sub-acute spinal cord injury	Spinal cord injury	Intrathecal transplantation of umbilical cord-MSC	2018
Intrathecal transplantation of UC-MSC in patients with late stage of chronic spinal cord injury	Spinal cord injuries	Umbilical cord mesenchymal stem cells	2018
Adipose stem cells for traumatic spinal cord injury	Spinal cord injuries; paralysis	Adipose stem cells	2018
Intrathecal administration of expanded Wharton's jelly mesenchymal stem cells in chronic traumatic spinal cord injury	Spinal cord injury, chronic	Wharton's jelly mesenchymal stem cells	2016
Transplantation of autologous bone marrow or leukapheresis-derived stem cells for treatment of spinal cord injury	Spinal cord injury	Transplantation of autologous bone marrow-derived stem cells	2016

(continued)

Table 9.7 (continued)

Title of trial	Disease	Type of stem cells	Year
NeuroRegen Scaffold™ combined with stem cells for chronic spinal cord injury repair	Spinal cord injury	NeuroRegen Scaffold™ combined with stem cells	2016
NeuroRegen Scaffold™ With bone marrow mononuclear cells transplantation versus intradural decompression and adhesiolysis in SCI	Spinal cord injury	NeuroRegen Scaffold™ with bone marrow mononuclear cells transplantation	2016

List of Clinical Trials in Peripheral Nerves Diseases

Forty-six clinical trials are being conducted using different types of stem cells to treat peripheral nerve diseases as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The list of trials conducted during the year 2016–2020 is listed in Table 9.8.

Table 9.8 List of clinical trials in peripheral nerve diseases

Title of trial	Disease	Type of stem cells	Year
BMAC nerve allograft study condition: peripheral nerve injury upper limb	Peripheral nerve injury upper limb	Bone marrow autologous cell nerve allograft	2019
A study to evaluate transplantation of astrocytes derived from human embryonic stem cells, in patients with amyotrophic lateral sclerosis (ALS)	ALS (amyotrophic lateral sclerosis)	Transplantation of astrocytes derived from human embryonic stem cells	2018
Intrathecal autologous adipose-derived mesenchymal stromal cells for amyotrophic lateral sclerosis (ALS)	Amyotrophic lateral sclerosis	Intrathecal autologous adipose-derived mesenchymal stromal cells	2017
Safety/efficacy study of 2nd cycle treatment after 6 months of 1st cycle HLA-haplo matched allogeneic bone marrow-derived stem cell treatment in ALS	Amyotrophic lateral sclerosis	HLA-haplo matched allogeneic bone marrow-derived stem cell	2017

(continued)

Table 9.8 (continued)

Title of trial	Disease	Type of stem cells	Year
Safety assessment of intravitreal mesenchymal stem cells for acute non-arteritic anterior ischemic optic neuropathy	Non-arteritic ischemic optic neuropathy	Mesenchymal stem cells	2017
Bone marrow-derived autologous stem cells for the treatment of Duchenne muscular dystrophy	Duchenne muscular dystrophy	Bone marrow-derived autologous stem cells	2017
Adipose stem/stromal cells in fibromyalgia, reflex sympathetic dystrophy, complex regional pain syndrome type i; fibromyalgia	Reflex sympathetic dystrophy); CRPS—complex regional pain syndrome type i; fibromyalgia	Adipose stem/stromal cells	2016
Study of two intrathecal doses of autologous mesenchymal stem cells for amyotrophic lateral sclerosis	Amyotrophic lateral sclerosis	Autologous mesenchymal stem cells	2016
Escalated application of mesenchymal stem cells in amyotrophic lateral sclerosis patients	Motor neuron disease	Mesenchymal stem cells	2016
Neurologic stem cell treatment study	Neurologic disorders	Intravenous bone marrow stem cells; procedure: intranasal bone marrow stem cells	2016

Clinical Trials of Heart Diseases with Stem Cell Therapy

Stem cells are tested as the treatment for various heart-related diseases and injuries. There are many clinical trials either currently in progress or have been completed where stem cells have been used in heart diseases as per the USA clinical trials portals.

List of Clinical Trials in Myocardial Infarction

Ninety-six clinical trials are being conducted using different stem cells in the treatment of myocardial infarction as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The list of trial which has been conducted during the year 2017–2020 are listed in Table 9.9.

Table 9.9 List of clinical trials in myocardial infarction

Title of trial	Disease	Type of stem cells	Year
WJMSCs anti-inflammatory therapy in coronary artery disease	Coronary artery disease	Wharton's jelly-derived mesenchymal stem Cell	2020
Stem cell in acute myocardial infarction	Acute myocardial infarction	Stem cells	2020
Evaluate the safety and explore efficacy of umbilical cord mesenchymal stem cells in acute myocardial infarction condition: acute myocardial infarction	Acute myocardial infarction	Umbilical cord mesenchymal stem cells	2020
MCRcI® stem cell treatment for diffuse coronary artery disease	Coronary artery disease	MCRcI® stem cell treatment	2019
MiSaver® stem cell treatment for heart attack (acute myocardial infarction)	Myocardial infarction	MiSaver® stem cell	2019
Serial infusions of allogeneic mesenchymal stem cells in ischemic cardiomyopathy patients with left ventricular assist device	Ischemic heart disease	Allogeneic mesenchymal stem cells	2019
UC-MSC transplantation for left ventricular dysfunction after AMI	Left ventricular dysfunction; acute myocardial infarction	Umbilical cord mesenchymal stem cell transplantation for	2019
Pericardial matrix with mesenchymal stem cells for the treatment of patients with infarcted myocardial tissue	Myocardial infarction	Pericardial matrix with mesenchymal stem cells	2019
First in humans to evaluate collagen patches with stem cells in patients with ischemic left ventricular dysfunction	Heart failure with reduced ejection fraction	Collagen patches with stem cells	2019
Evaluate the safety and explore efficacy of umbilical cord mesenchymal stem cells with acute myocardial infarction	Acute myocardial infarction	Umbilical cord mesenchymal stem cells	2018

(continued)

Table 9.9 (continued)

Title of trial	Disease	Type of stem cells	Year
Sequential treatment of extra-corporeal shock wave combined with autologous bone marrow mesenchymal stem cells on patients with ischemic heart disease	Ischemic heart disease	Treatment of extra-corporeal shock wave combined with autologous bone marrow mesenchymal stem cells	2018
ICBMC-MI. Intracoronary bone marrow mononuclear cells in myocardial infarction (MI) patients	Heart failure	Intracoronary bone marrow mononuclear cells	2017
Transplantation efficacy of autologous bone marrow mesenchymal stem cells with intensive atorvastatin in AMI patients	Myocardial infarction	Autologous bone marrow mesenchymal stem cells	2017

List of Clinical Trials in Stroke and Related Diseases

There are 66 clinical trials being conducted using different types of stem cells in stroke and related disease treatment as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The trial list conducted during the year 2017–2020 is listed in Table 9.10.

Table 9.10 List of clinical trials in stroke and related diseases

Title of trial	Disease	Type of stem cells	Year
Evaluate the safety and explore efficacy of umbilical cord mesenchymal stem cells in acute ischemic stroke	Acute stroke	Umbilical cord mesenchymal stem cells	2020
Allogeneic adipose tissue-derived mesenchymal stem cells in ischemic stroke conditions: ischemic stroke	Ischemic stroke	Allogeneic adipose tissue-derived mesenchymal stem cells	2020
Mesenchymal stem cells for the treatment of acute ischemic stroke	Acute ischemic stroke	Mesenchymal stem cells	2019
Effect of different transplantation time for mesenchymal stem cells (MSCs) of cerebral infarction patients	Infarction, middle cerebral artery	Mesenchymal stem cells (MSCs)	2019

(continued)

Table 9.10 (continued)

Title of trial	Disease	Type of stem cells	Year
An open-labeled phase ii study to evaluate the efficacy and safety of GXNPC-1 (autologous adipose-derived stem cells) in patients with chronic stroke condition: chronic stroke	Chronic stroke	Autologous adipose-derived stem cells	2019
Combination therapy of umbilical cord blood and erythropoietin for stroke patients	Stroke	Combination therapy of umbilical cord blood with erythropoietin	2019
Regenerative stem cell therapy for stroke in Europe	Stroke	Regenerative stem cell therapy	2018
MultiStem® administration for stroke treatment and enhanced recovery study	Ischemic stroke	MultiStem® administration	2018
Allogeneic mesenchymal stem cell-derived exosome in patients with acute ischemic stroke	Cerebrovascular disorders	Allogeneic mesenchymal stem cell-derived exosome	2017
Mesenchymal stem cells therapy in patients with recent intracerebral hemorrhage	Hemorrhagic stroke	Mesenchymal stem cells therapy	2017
The safety and efficacy of human umbilical cord mesenchymal stem cells in the treatment of acute cerebral infarction	Cerebral infarction	Human umbilical cord mesenchymal stem cells	2017
Human umbilical cord mesenchymal stem cell therapy for cerebral infarction patients in convalescent period	Cerebral infarction	Human umbilical cord mesenchymal stem cell therapy	2017
Role of umbilical cord milking in the management of hypoxic-ischemic encephalopathy in neonates	Role of hypoxic-ischemic encephalopathy	Umbilical cord milking	2017

List of Clinical Trials in Digestive System Diseases

There are 90 clinical trials being conducted using different types of stem cells to treat digestive system diseases as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The trial list conducted during the year 2017–2020 is listed in Table 9.11.

Table 9.11 List of clinical trials in digestive system diseases

Title of trial	Disease	Type of stem cells	Year
Study of mesenchymal stem cells for the treatment of medically refractory Crohn's colitis	Crohn's colitis	Mesenchymal stem cells	2020
Study of mesenchymal stem cells for the treatment of medically refractory ulcerative colitis (UC)	Ulcerative colitis	Mesenchymal stem cells	2020
Mesenchymal stem cells for the treatment of rectovaginal fistula in participants with Crohn's disease	Rectovaginal fistula; Crohn's disease	Mesenchymal stem cells	2020
Study of mesenchymal stem cells for the treatment of ileal pouch fistula's in participants with Crohn's disease	Ileal pouch; Crohn's disease	Mesenchymal stem cells	2020
Mesenchymal stem cells for the treatment of perianal fistulizing Crohn's Disease Conditions: perianal Crohn's disease	Perianal Crohn's disease	Mesenchymal stem cells	2020
Umbilical cord mesenchymal stem cell for liver cirrhosis patient caused by hepatitis B	Liver cirrhosis	Umbilical cord mesenchymal stem cell	2020
Angiographic delivery of AD-MSC for ulcerative colitis Condition: ulcerative colitis Intervention: drug: adipose-derived, autologous mesenchymal stem cells	Ulcerative colitis	Adipose-derived, autologous mesenchymal stem cells	2020
Combination of autologous MSC and HSC infusion in patients with decompensated cirrhosis	Cirrhosis, liver	Combination of autologous MSC and HSC Infusion	2020
A phase II open-label single-arm study to evaluate the efficacy and safety of autologous adipose-derived stem cells (ADSCs) in subjects with liver cirrhosis Condition: liver cirrhosis	Liver cirrhosis	Autologous adipose-derived stem cells	2019

(continued)

Table 9.11 (continued)

Title of trial	Disease	Type of stem cells	Year
Mesenchymal stem cells for the treatment of pouch fistulas in Crohn's	Crohn's disease	Mesenchymal stem cells	2019
Evaluation of local co-administration of autologous ADIpose-derived stromal vascular fraction with microfat for refractory perianal Crohn's Fistula	Crohn's disease	Co-administration of autologous adipose-derived stromal vascular fraction	2019
Mesenchymal stem cells treatment for decompensated liver cirrhosis Condition: Decompensated liver cirrhosis Interventions: biological: umbilical cord-derived mesenchymal stem cell;	Decompensated liver cirrhosis	Mesenchymal stem cells—umbilical cord-derived mesenchymal stem cell	2019
MSC intra-articular injection in Crohn's disease patients Condition: efficacy and safety Intervention: biological: mesenchymal stromal cells	Crohn's disease	Mesenchymal stromal cells	2019
Allogeneic ABCB5-positive stem cells for treatment of acute-on-chronic liver failure Condition: acute-on-chronic liver failure	Acute-on-chronic liver failure	Allogeneic ABCB5-positive stem cells	2019
Clinical study of human umbilical cord mesenchymal stem cells in the treatment of decompensated hepatitis b cirrhosis	Hepatitis B	Human umbilical cord mesenchymal stem cells	2019
Mesenchymal stem cell transplantation for refractory primary biliary cholangitis Condition: primary biliary cirrhosis	Primary biliary cirrhosis	Mesenchymal stem cell transplantation	2018

(continued)

Table 9.11 (continued)

Title of trial	Disease	Type of stem cells	Year
Mesenchymal stem cell transplantation for acute-on-chronic liver failure Condition: acute-on-chronic liver failure	Acute-on-chronic Liver failure	Mesenchymal stem cell transplantation	2018
Clinical trial of umbilical cord mesenchymal stem cell transfusion in decompensated liver cirrhosis	Decompensated liver cirrhosis	Umbilical cord mesenchymal stem cell	2018
Stem cells treatment of complex Crohn's anal fistula Conditions: anal fistula	Anal fistula	Stem cells treatment	2018
Safety and efficacy study of mesenchymal stem cell in treating liver fibrosis	Liver cirrhosis	Mesenchymal stem cell	2018
Adult allogeneic expanded adipose-derived stem cells (eASC) for the treatment of complex perianal fistula(s) in patients with Crohn's disease	Crohn's disease	Adult allogeneic expanded adipose-derived stem cells	2017

List of Clinical Trials in Eye Diseases

There are 90 clinical trials are being conducted using different types of stem cells in the treatment of in eye diseases as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The list of trial which has been conducted during year 2017–2020 is listed in Table 9.12**.**

List of Clinical Trials in Kidney Diseases

There are 47 clinical trials being conducted using different types of stem cells to treat kidney diseases as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The trial list conducted during the year 2017–2020 is listed in Table 9.13.

Table 9.12 List of clinical trials in eye diseases

Title of trial	Disease	Type of stem cells	Year
Autologous transplantation of induced pluripotent stem cell-derived retinal pigment epithelium for geographic atrophy associated with age-related macular degeneration	Age-related macular degeneration	Autologous transplantation of induced pluripotent stem cell-derived retinal pigment epithelium	2020
Effect of UMSCs-derived exosomes on dry eye in patients with cGVHD Condition: dry eye	Dry eye	Umbilical mesenchymal stem cells-derived exosomes	2020
Treatment of central retinal vein occlusion using stem cells study Condition: central retinal vein occlusion	Treatment of central retinal vein occlusion	Autologous bone marrow CD34+ stem cells	2019
Interventional study of implantation of hESC-derived RPE in patients with rp due to monogenic mutation Condition: retinitis pigmentosa Intervention: biological: human embryonic stem cell-derived retinal pigment epithelium (RPE)	Retinitis pigmentosa	Human embryonic stem cell-derived retinal pigment epithelium (RPE)	2019
Safety and efficacy of subretinal transplantation of clinical human embryonic stem cell-derived retinal pigment epitheliums in treatment of retinitis pigmentosa	Retinitis pigmentosa	Human embryonic stem cell-derived retinal pigment epitheliums	2019
Treatment with allogeneic adipose-derived mesenchymal stem cells in patients with aqueous deficient dry eye disease	Dry eye	Allogeneic adipose-derived mesenchymal stem cells	2018
Corneal epithelial stem cells and dry eye disease Conditions: dry eye syndromes; dry eye; ocular inflammation; ocular surface disease; ocular discomfort; blepharitis	Inflammation; ocular surface disease; ocular discomfort; blepharitis	Corneal epithelial stem cells	2017

(continued)

Table 9.12 (continued)

Title of trial	Disease	Type of stem cells	Year
Safety assessment of intravitreal mesenchymal stem cells for acute non-arteritic anterior ischemic optic neuropathy	Non-arthritic ischemic optic neuropathy	Mesenchymal stem cells	2017
Treatment of dry age-related macular degeneration disease	Dry age-related macular degeneration	Retinal pigment epithelium derived from clinical-grade human embryonic stem cells	2017

Table 9.13 List of clinical trials in kidney diseases

Title of trial	Disease	Type of stem cells	Year
Clinical research of UC-MSCs in the treatment of diabetic nephropathy	Diabetic nephropathy	Umbilical cord-mesenchymal stem cells	2020
Clinical study of umbilical cord mesenchymal stem cells in the treatment of type 2 diabetic nephropathy	Type 2 diabetes with renal manifestations	Umbilical cord mesenchymal stem cells	2020
Clinical trial of mesenchymal stem cells in the treatment of severe acute kidney injury	Acute kidney injury; mesenchymal stem cells	Mesenchymal stem cells	2020
Cell-based therapy for the treatment of kidney disease Condition: kidney diseases	Kidney diseases	Cell-based therapy—endothelial progenitor cell	2019
Umbilical cord mesenchymal stem cells therapy for diabetic nephropathy	Diabetic nephropathy	Umbilical cord mesenchymal stem cells	2019
Safety and efficacy study of mesenchymal stem cell in treating kidney fibrosis	Renal cirrhosis	Mesenchymal stem cell	2018
Treatment of chronic renal failure with adipose tissue-derived mesenchymal stem cells Conditions: mesenchymal stem cells; chronic kidney diseases; renal interstitial fibrosis	Chronic kidney diseases; renal interstitial fibrosis	Adipose tissue-derived mesenchymal stem cells	2018
Use of Wharton's jelly in diabetic nephropathy	Diabetic nephropathy	Wharton's jelly mesenchymal stem cells	2017
Adipose-derived stem cells (ADSCs) for moderate to severe chronic kidney disease	Moderate to severe chronic kidney disease	Adipose-derived stem cells (ADSCs)	2016

(continued)

Table 9.13 (continued)

Title of trial	Disease	Type of stem cells	Year
AMSCs in reducing hemodialysis arteriovenous fistula failure Conditions: end stage renal disease (ESRD); vascular access complication	End stage renal disease	Adipose-derived mesenchymal stem cells (AMSC)	2016

List of Clinical Trials in Skin Diseases

There are 47 clinical trials in skin diseases as per the USA clinical trials portals (https://www.clinicaltrials.gov/) and (https://stemcellsportal.com/stem-cells-translational-medicine-clinical-trials-portal). The trial list conducted during the year 2017–2020 is listed in Table 9.14.

Table 9.14 List of clinical trials in skin diseases

Title of trial	Disease	Type of stem cells	Year
Human placental mesenchymal stem cells treatment on diabetic foot ulcer	Diabetic foot ulcer	Human placental mesenchymal stem cells	2020
Subcutaneous injections of autologous ASC to heal digital ulcers in patients with scleroderma	Systemic sclerosis	Autologous adult stem cells	2020
Phase 1, open-label safety study of umbilical cord lining mesenchymal stem cells (corlicyte®) to heal chronic diabetic foot ulcers	Diabetic foot ulcer	Umbilical cord lining mesenchymal stem cells	2019
Clinical study of adipose-derived stem cells in the treatment of diabetic foot	Diabetes mellitus foot ulcer	Adipose-derived stem cells	2019
Therapy of scars and cutis laxa with autologous adipose-derived mesenchymal stem cells Conditions: skin; scar; cutis laxa; keloid; cicatrix	Skin; scar; cutis laxa; keloid; cicatrix	Autologous adipose-derived mesenchymal stem cells	2019

(continued)

Table 9.14 (continued)

Title of trial	Disease	Type of stem cells	Year
Treatment of chronic wounds in diabetic foot syndrome with autologous adipose-derived mesenchymal stem cells	Diabetic foot ulcer	Autologous adipose-derived mesenchymal stem cells	2019
Clinical research on treatment of psoriasis by human umbilical cord-derived mesenchymal stem cells	Psoriasis	Human umbilical cord-derived mesenchymal stem cells	2018
Long term effects on skin hyper pigmentation with and without mesenchymal stem cell enriched adipose tissue grafting for "contour deformities with pigmentary changes on face" Conditions: skin pigmentation over contour deformities of Fac	Skin pigmentation over contour deformities of face	Mesenchymal stem cell enriched adipose tissue grafting	2018
A randomized, positive controlled trial assess the efficacy and safety of Uc-MSC in plaque psoriasis patients	Moderate and severe plaque psoriasis	Umbilical cord-mesenchymal stem cells	2018

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