



204 Executive Court
Little Rock, AR 72205
501-444-2385

<https://mdvisitclinic.com/stem-cells-arkansas/>

Human Umbilical Cord Mesenchymal Stem Cell Delayed Renal Chronic Kidney Disease (CKD3,4)

ClinicalTrials.gov ID NCT05512988

Sponsor Tongji Hospital

Information provided by Gang Xu, Tongji Hospital (Responsible Party)

Last Update Posted 2022-08-23

Study Overview

Brief Summary

The chronic kidney disease is caused by renal structural and functional impairment for more than 3 months due to various causes, including normal and abnormal glomerular filtration rate (GFR), abnormal blood, urine, and imaging findings, or an unexplained decline in GFR (<60 ml/min). Recent years, the incidence of chronic kidney disease has increased year by year worldwide, the incidence of CKD is 8% to 16% in the world's total population. chronic kidney disease has become an important public health problem in China and even the world.

Summarizing the basic and clinical studies at home and abroad, inflammatory factors such as inflammatory chemokines, cytokines, and reactive oxygen species interact with fibrosis factors such as mesangial cells, fibroblasts, and fibroblast activation, which are the root causes of the progression of CKD and the formation of tubular interstitial fibrosis and glomerular sclerosis and developing into end-stage renal disease.

OBSERVATIONAL RESEARCH ON AN EXPERIMENTAL USE PARADIGM

Current treatments for chronic kidney disease are very limited, and to be precise, there is currently no cure for chronic kidney disease, nor is there a proven way to improve the kidneys survive after acute kidney injury (AKI). **The progression of the disease itself can only be delayed as much as possible by changing the diet, controlling related complications with oral medications (such as hypertension, hyperlipidemia, nephropathy, etc.), and actively controlling blood glucose and glycosylated hemoglobin levels in patients with diabetes.** For patients with stage CKD5 and more severe, renal replacement therapy is recommended, including hemodialysis and peritoneal dialysis, but there are many complications in both dialysis methods, such as narrowing of the internal fistula, occlusion, catheter infection, peritonitis, etc. Kidney transplantation may be considered when economic conditions permit and there is a matching kidney source, but kidney transplant surgery is riskier. The above treatment methods have brought a heavy burden to patients and social medicine. **In order to seek innovative and effective strategies to cultivate the limited regenerative capacity of the kidneys and reverse renal fibrosis, the mesenchymal stem cells (MSCs) with tissue regenerative potential and immunomodulatory functions have brought new ideas and hopes for the prevention and treatment of chronic kidney disease.**

Detailed Description

The chronic kidney disease is caused by renal structural and functional impairment for more than 3 months due to various causes, including normal and abnormal glomerular filtration rate (GFR), abnormal blood, urine, and imaging findings, or an unexplained decline in GFR (<60 ml/min). Recent years, the incidence of chronic kidney disease has increased year by year worldwide, the incidence of CKD is 8% to 16% in the world's total population. The incidence of CKD and the primary causative factors vary from country to country and region, and the idemiological survey led by Peking University Hospital shows that the prevalence of CKD in China is 10.8% , the primary causative factor is glomerulonephritis, but as the incidence of hypertension and diabetes rises year by year, and the world will have more than 10 million people a year have acute kidney injury, the proportion of chronic kidney disease in the long-term course of the above population will be much higher than the normal population, chronic kidney disease has become an important public health problem in China and even the world.

OBSERVATIONAL RESEARCH ON AN EXPERIMENTAL USE PARADIGM

Summarizing the basic and clinical studies at home and abroad, inflammatory factors such as inflammatory chemokines, cytokines, and reactive oxygen species interact with fibrosis factors such as mesangial cells, fibroblasts, and fibroblast activation, which are the root causes of the progression of CKD and the formation of tubular interstitial fibrosis and glomerular sclerosis and developing into end-stage renal disease.

Current treatments for chronic kidney disease are very limited, and to be precise, there is currently no cure for chronic kidney disease, nor is there a proven way to improve the kidneys survive after acute kidney injury (AKI). The progression of the disease itself can only be delayed as much as possible by changing the diet, controlling related complications with oral medications (such as hypertension, hyperlipidemia, nephropathy, etc.), and actively controlling blood glucose and glycosylated hemoglobin levels in patients with diabetes. For patients with stage CKD5 and more severe, renal replacement therapy is recommended, including hemodialysis and peritoneal dialysis, but there are many complications in both dialysis methods, such as narrowing of the internal fistula, occlusion, catheter infection, peritonitis, etc. The presence of the above complications will reduce the service life of the patient's dialysis pathway while also causing blows to other organ systems. Kidney transplantation may be considered when economic conditions permit and there is a matching kidney source, but kidney transplant surgery is riskier, and the average survival of transplanted kidneys is currently 12 years calculated by the American National Kidney Foundation, during this period, patients need to take anti-rejection drugs uninterruptedly, and these drugs (such as tacrolimus, cyclosporine, etc.) can also greatly damage the kidney organs and function. The above treatment methods have brought a heavy burden to patients and social medicine. In order to seek innovative and effective strategies to cultivate the limited regenerative capacity of the kidneys and reverse renal fibrosis, the mesenchymal stem cells (MSCs) with tissue regenerative potential and immunomodulatory functions have brought new ideas and hopes for the prevention and treatment of chronic kidney disease.

Progression in chronic kidney disease includes tubular interstitial fibrosis and glomerulosclerosis:

- 1) Tubular interstitial fibrosis is mainly characterized by tubular hypermetabolism, tubular epithelial-interstitial transition, and hypoxic damage to the renal interstitium, which eventually leads to infiltration of inflammatory cells, abnormal increase in extracellular matrix components in renal tissue, and disappearance of parenchymal cells.

OBSERVATIONAL RESEARCH ON AN EXPERIMENTAL USE PARADIGM

2) Glomerulosclerosis is the outcome of excessive response of glomerular constituent related cells to injury, including structural changes, cells' gradual atrophy, shedding, apoptosis of cells, loss of anticoagulant properties, and increased expression of pro-inflammatory factors and pro-fibrosis factors; Proliferation of mesangial cells, mesangial differentiation into myofibroblasts, causing collagen III to be deposited in the renal units, leading to irreversible hardening of the glomeruli; The number of pinus process cells decreases, the skeleton retracts or flattens, and inflammatory cell aggregation of chemokines is released, while synthetic cytokines and growth factors further aggravate globules capillary sclerosis.

Both pathophysiological abnormalities are characterized by parenchymal cell loss and activation of the inflammatory immune response. However, due to the weak regenerative capacity of renal tubular epithelial cells and endothelial cells, foot process cells even lack regenerative ability, these renal parenchymal cells are difficult to repair themselves once damaged, and the kidney lacks stem/progenitor cells, which cannot achieve stem/progenitor cell differentiation and regeneration. Therefore, after severe kidney damage, the existing treatment methods cannot promote the complete repair of the kidneys, often resulting in the delay of kidney disease, which is also the main reason why chronic kidney disease has become the highest incidence of chronic disease in humans.

MSCs are only briefly present in the renal vascular system, and Togel F, Hu Z et al. found that their presence was not detected within the renal parenchyma after 3 days of MSC infusion, and in general, stem cells were only briefly present in the blood vessels of the kidneys and could not colonize for long periods of time 7. **Studies such as Camila Eleuterio Rodrigues found that gene expression in the kidneys of MSC-treated rats showed a decrease in pro-inflammatory cytokines and an increase in several growth factors with pro-mitosis, pro-survival, and anti-apoptosis effects**8. **There is a large body of research evidence that MSCs modulate the immune response primarily through paracrine/endocrine nutritional growth factors and ultimately promote renal repair.**

1) Stem cells secrete immunomodulatory correlates;

2) Stem cell secretion promotes renal vascular formation and tubular cell regeneration related factors;

OBSERVATIONAL RESEARCH ON AN EXPERIMENTAL USE PARADIGM

- 3) MSC may also reduce renal fibrosis and structural remodeling through immunomodulation;
- 4) Stem cell secretion improves matrix metabolism-related factors.

Mesenchymal stem cell therapy has a good safety record, there is no obvious toxic side effects for patients, a small number of patients have injection of local discomfort, transient low-grade fever, etc., generally do not need special treatment, patients will recover naturally, long-term observation has not found that patients have increased microbial infections and the carcinogenicity of Mesenchymal stem cell.

Characteristics and advantages of umbilical cord mesenchymal stem cells, MSCs isolated from umbilical cord tissue, not only maintain the biological characteristics of MSCs, but also have the following advantages compared to other tissue-derived mesenchymal stem cells: 1) Convenient materials, which is waste utilization. 2) The process is less invasive to the donor than the extraction of bone marrow MSCs. 3) The isolated cell content and proliferation ability are better than bone marrow MSCs, and the immunogenicity is lower than that of bone marrow MSCs, which is not easy to trigger the immune response or cause graft-versus-host disease. 4) The differentiation potential is stronger, and differentiation can be carried out in multiple directions. 5) Stronger ability to secrete cytokines and may have a stronger paracrine (exosome) repair effect. 6) Compared with bone marrow MSCs, the results of gene lineage comparison show that umbilical cord mesenchymal stem cells can express more genes and proteins related to matrix remodeling and angiogenesis, which is more suitable in the field of nephropathy treatment.

Therefore, in the field of nephropathy treatment, umbilical cord MSC has greater potential for application.

This study was a prospective, single center, randomized controlled and double-blind study, total duration 36 months, of which each patient study cycle is 13 months, and long-term safety follow-up is 12 months after the end of the study. It is grouped by the random number table method, divided into the experimental group and the control group according to the ratio of 1:1, 22 people were required in the experimental group and 22 people in the control group, for a total of 44 people. Experimental group will receive UC-MSC, while the control group will receive saline solution. The expected effect is UC-MSC can delay the progression of renal function in patients with brady nephropathy, reduced or alleviated chronic kidney disease-related complications (e.g., anemia, hypertension).

OBSERVATIONAL RESEARCH ON AN EXPERIMENTAL USE PARADIGM

Official Title

A Randomized, Double-blind, Controlled Clinical Study of Human Umbilical Cord
Mesenchymal Stem Cell(UC-MSC)Delayed Renal Chronic Kidney Disease(CKD3, 4)