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Using Nanotechnology in Kidney Treatment

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Abstract

Glomerulonephritis (GN) is a group of inflammatory diseases characterized by glomerular injury and lesions. The causes of GN are relatively complex, and the pathogenesis is not yet clear. It may be caused by autoimmune dysfunction or may be related to multiple factors, such as genetics, infection, drugs, viruses, and the environment. GN can be divided into primary and secondary GN in terms of etiology . Common pathological types of primary GN include acute GN, crescentic GN, membranous GN, membranoproliferative GN, mesangial proliferative GN, focal segmental glomerulosclerosis (FSG), minimal change GN, IgA nephropathy (IgAN) and chronic GN. The most common types of secondary GN include diabetic nephropathy (DN) and lupus nephritis (LN). The symptoms of GN vary widely. Many patients have no special symptoms in the early stage. Some patients present with nephritic syndrome (hematuria, proteinuria, edema and hypertension), and some patients show nephrotic syndrome (hyperlipidemia, severe edema, heavy proteinuria and hypoproteinemia). Even patients with the same pathological characteristics may exhibit varying degrees of proteinuria However, some typical clinical manifestations can correspond to specific GN. After 1–4 weeks of streptococcal infection, patients with symptoms such as edema, hypertension, and hematuria can be diagnosed with acute GN. Recurrent episodic microscopic or macroscopic hematuria is a landmark clinical feature of IgAN, which is the most common primary GN in the world.

Keywords: Nanotechnology, Kidney, Treatment

Introduction

Nanotechnology has extensive application as Nano medicine in the medical field. Some nanoparticles have possible applications in novel diagnostic instruments, imagery and methodologies, targeted medicinal products, pharmaceutical products, biomedical implants, and tissue engineering. Today treatments of high toxicity can be administered with improved safety using nanotechnology, such as chemotherapeutic cancer drugs. Further, wear-able gadgets can detect crucial changes in vital signs, cancer cell conditions, and infections that are genuinely happening in the body. We anticipate these technologies to provide doctors with considerably much better direct access to critical data on the reasons for changes in the signs of life or illness because of the technological presence at the source of the problem. Biomedicine can be utilized for therapies with predictive analytics and artificial intelligence. Glomerulonephritis (GN) is the most common cause of end-stage renal failure worldwide; in most cases, it cannot be cured and

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can only delay the progression of the disease. At present, the main treatment methods include symptomatic therapy, immunosuppressive therapy, and renal replacement therapy. However, effective treatment of GN is hindered by issues such as steroid resistance, serious side effects, low bioavailability, and lack of precise targeting. With the widespread application of nanoparticles in medical treatment, novel methods have emerged for the treatment of kidney diseases. Targeted transportation of drugs, nucleic acids, and other substances to kidney tissues and even kidney cells through nanodrug delivery systems can reduce the systemic effects and adverse reactions of drugs and improve treatment effectiveness. The high specificity of nanoparticles enables them to bind to ion channels and block or enhance channel gating, thus improving inflammation. This review briefly introduces the characteristics of GN, describes the treatment status of GN, systematically summarizes the research achievements of nanoparticles in the treatment of primary GN, diabetic nephropathy and lupus nephritis, analyzes recent therapeutic developments, and outlines promising research directions, such as gas signaling molecule nanodrug delivery systems and ultrasmall nanoparticles.

The structural basis of the kidney as a multi-potential target organ for treatment

The kidney consists of approximately one million nephrons, including glomeruli with filtration function and renal tubules with reabsorption function, with a complex structure and various cell types, pathological features of CKD or AKI. It regulates aspects such as the body's water and electrolyte balance, excretion of metabolic waste, and the regulation of acid-base and blood pressure, all of which can serve as potential targets for treatment. Nanocarrier materials for drug delivery mainly include active targeting, passive targeting, and other mechanisms for targeting the kidneys.

The renal unit is the fundamental unit of kidney structure and function. Each renal unit consists of the renal corpuscle and renal tubules. The renal corpuscle is composed of the glomerulus and the urinary space. The glomerulus consists of capillaries, while the urinary space is a double-layered capsule surrounding the glomerulus, with the outer layer being the parietal layer and the inner layer being the visceral layer. The parietal layer contains parietal epithelial cells, the visceral layer has podocytes, and endothelial cells are on the capillary lumen's side. A basement membrane separates the endothelial cells and podocytes, and mesangial cells and mesangial matrix connect adjacent capillaries. These three layers form the filtration barrier. The glomerular vessel pole has a macula dense.

Characteristics of nanogels

Firstly, biocompatibility and biodegradability. In studies using injectable nanogels for treating bone and joint injuries, no inflammatory reactions were observed, confirming the excellent biocompatibility of nanogels . Nanogels can be modified or compounded to create high-performance nanogels with biodegradability, showing great potential in applications for implants and drug delivery . Secondly, swelling and water absorption properties. Nanogels can absorb large amounts of water due to the presence of hydrophilic groups in the main chain or end chains of the polymer material, with a water content of up to 99%. When used as medical dressings, nanogels can absorb wound exudate while maintaining a moist environment, adhering closely to the wound without causing adhesion, reducing bacterial contact, and preventing secondary trauma . Additionally, they exhibit stimulus responsiveness. Nanogels, with high water content, high sensitivity, and controllable structure and physicochemical properties, can respond rapidly to external environmental stimuli through swelling, contraction, or sol-gel phase transition. Based on the different stimuli that trigger the response, the stimulus responsiveness of nanogels can be classified as a physical response and a chemical response. Physical response refers to the nanogels's response to changes in the physical environment, such as thermal response, light response, magnetic field response, and mechanical response .Chemical response refers to the nanogels's response to changes in the chemical environment, such as pH and ionic strength.

Application of polymer nanogels in kidney disease

Hydrogels, as a delivery system for biomedical materials, are typically used to deliver drugs smaller than 15 nm, such as small molecule drugs or small proteins. Generally, drug-loaded hydrogels primarily release through diffusion, and controlled drug release can be achieved by controlling the hydrogel network's degradation, swelling, and mechanical deformation . Hydrogels can serve as carriers to transport growth factors, anti-inflammatory drugs safely, and even stem cell therapy for acute kidney injury (AKI). Substantial research evidence supports hydrogel carriers' direct targeted drug delivery capability, such as the significant effectiveness and biocompatibility of counteracting oxidative stress-driven mechanisms (such as inflammatory signals and mitochondrial damage). These studies provide encouraging evidence for the potential therapeutic value of hydrogel drug delivery.

Nanoparticles and renal anemia

Oral or intravenous iron drops are primarily used to treat renal anemia. Ferumoxytol is a new, semisynthetic, carbohydrate-coated, superparamagnetic iron oxide nanoparticle that can be administered intravenously. It produces the least dialyzable free iron and can release free iron more stably than the other iron products. Therefore, its bioavailability is better than that of oral administration, and its tolerance is better, with fewer side effects . Many randomized controlled trials and cohort studies have shown that it is more effective than oral iron in improving anemia and can increase transferrin saturation (TSAT) and ferritin levels. The probability of most adverse events is similar to that of other oral iron . A higher risk of hypotension may be associated with fewer adverse gastrointestinal events . However, Ferumoxytol received a black box warning from the FDA in March 2015, reminding doctors to pay attention to the possibility of hypersensitivity reactions, including allergic reactions. Therefore, it is necessary to reduce the infusion rate.

Application of nanoparticles in dialysis

Renal failure was defined as a glomerular filtration rate of <15 mL/min/1.73 m2 . Dialysis is one of the main treatment methods for patients with renal failure , and the number of dialysis patients has gradually increased over the last 20 years. Although dialysis treatment has become increasingly developed, the mortality rate of patients undergoing dialysis remains very high . Various complications may arise as a result of dialysis, such as cardiovascular events, catheter-related infections, peritonitis, among others. In addition, dialysis may cause great inconvenience to patients, especially those undergoing hemodialysis, because a dialysis frequency of three times/week may result in patients risking unemployment to attend dialysis appointments . The increase in economic burden causes the disease burden on patients to rise continuously ; thus, our goal is to make dialysis technology safer, more efficient, and more convenient. Nanotechnology can be used as a new method for treating arteriovenous fistulas. Ferumoxytol is an iron-oxide nanoparticle that can be used as a substitute for MRI contrast agents. Ferumoxytol can identify the condition of the central artery, better identify peripheral artery diseases, and better predict the results of arteriovenous fistula surgery. One of the main obstacles to blood filtration is blockage caused by thrombosis, which limits the maximum filter life during hemodialysis and continuous renal replacement therapy . Dialysis membrane pores must be sufficiently small to prevent protein loss from plasma, and membrane surfaces should be carefully designed to provide high membrane blood compatibility and minimal thrombosis . Engineering changes in membrane surface chemistry and structure by doping with nanomaterials has attracted extensive attention. Ag nanoparticles and multiwalled carbon nanotubes (MWNT) may be the most important nanomaterials with blood compatibility and low toxicity to blood cells. For example, a gold nanoparticle-modified artificial kidney, which expresses a negatively charged surface, reduced some acute adverse effects caused by dialysis-induced protein adsorption, platelet adhesion, and coagulation activation, thus avoiding thrombosis during hemodialysis . In addition, an AuNP-modified Pt electrode was used to measure the relative loss of amino acids in patients undergoing renal replacement therapy by analyzing the amino acid levels in diluted serum samples before and after entering/leaving the hemodialysis apparatus.

Conclusion

The emergence of nanoparticles has brought hope to medicine. Regarding kidney disease, early potential patients and disease progression can be identified using gas measurements and urine detection. Magnetic nanoparticles can reduce the renal fibrosis caused by iodine or gadolinium contrast agents in patients with CKD. Gold nanoparticles and silica nanoparticles are also used for renal imaging to evaluate renal inflammation and fibrosis, and may become a tool to replace renal biopsy puncture in the future. CKD is associated with vascular and renal fibrosis. Albumin nanoparticles can target degraded elastin to reverse vascular calcification. While polymer nanoparticles can package and deliver related drugs to specific parts of the kidney to improve their bioavailability and half-life and effectively treat renal fibrosis, superparamagnetic iron oxide nanoparticles can be administered intravenously to treat renal anemia and appear to be more effective than traditional oral iron agents. In addition, during dialysis treatment, the use of gold nanoparticles can improve the chemical structure of the dialysis membrane, thus reducing the adverse reactions of thrombosis and detecting the loss of amino acids in patients after dialysis. In summary, many types of nanoparticles have been used for the diagnosis and treatment of patients with CKD; however, most trials are still in the preclinical stage, and nanoparticles have not been routinely used in clinical practice. We believe that the application of nanoparticles to patients with CKD is clinically meaningful, as it may allow for more accurate and effective diagnosis and treatment of CKD in the future.

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